10/736,004

EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	9	(methamphetamine and amphetamine and immunogenic and carrier and label and antibod$3).clm.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/07/25 15:07
L2	9	(methamphetamine and amphetamine and immunogenic and carrier and label and antibod$3).clm.	US-PGPUB; USPAT	OR	OFF	2006/07/25 15:04
L3	3	(zheng near1 feng or hsiou$1 near1 liu or Yali near1 yang) and (amphetamine or methamphetamine or antactogen$1)	US-PGPUB; USPAT	OR	OFF	2006/07/25 15:07
L4	3	(zheng near1 feng or hsiou$1 near1 liu or Yali near1 yang) and (amphetamine or methamphetamine or antactogen$1)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/07/25 15:07
L5	150	(methamphetamine or amphetamine or antactogen$1) same (immunogen$2 or label or tracer)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/07/25 15:09
L6	129	l5 and antibod$3	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT; IBM_TDB	OR	OFF	2006/07/25 15:09

10/736,004

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LOGINID:[redacted]

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TERMINAL (ENTER 1, 2, 3, OR ?):2


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 NEWS  1          Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2          "Ask CAS" for self-help around the clock
 NEWS  3  FEB 27  New STN AnaVist pricing effective March 1, 2006
 NEWS  4  APR 04  STN AnaVist $500 visualization usage credit offered
 NEWS  5  MAY 10  CA/CAplus enhanced with 1900-1906 U.S. patent records
 NEWS  6  MAY 11  KOREAPAT updates resume
 NEWS  7  MAY 19  Derwent World Patents Index to be reloaded and enhanced
 NEWS  8  MAY 30  IPC 8 Rolled-up Core codes added to CA/CAplus and
                  USPATFULL/USPAT2
 NEWS  9  MAY 30  The F-Term thesaurus is now available in CA/CAplus
 NEWS 10  JUN 02  The first reclassification of IPC codes now complete in
                  INPADOC
 NEWS 11  JUN 26  TULSA/TULSA2 reloaded and enhanced with new search and
                  and display fields
 NEWS 12  JUN 28  Price changes in full-text patent databases EPFULL and PCTFULL
 NEWS 13  JUl 11  CHEMSAFE reloaded and enhanced
 NEWS 14  JUl 14  FSTA enhanced with Japanese patents
 NEWS 15  JUl 19  Coverage of Research Disclosure reinstated in DWPI

 NEWS EXPRESS  JUNE 30 CURRENT WINDOWS VERSION IS V8.01b, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 26 JUNE 2006.

 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS LOGIN    Welcome Banner and News Items
 NEWS IPC8     For general information regarding STN implementation of IPC 8
 NEWS X25      X.25 communication option no longer available

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* * * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 14:22:30 ON 25 JUL 2006

=>
Uploading
THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE
Do you want to switch to the Registry File?
Choice (Y/n):
```

Switching to the Registry File...
Some commands only work in certain files. For example, the EXPAND command can only be used to look at the index in a file which has an index. Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of commands which can be used in this file.

=> FILE REGISTRY

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 14:23:06 ON 25 JUL 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 23 JUL 2006 HIGHEST RN 895579-80-3
DICTIONARY FILE UPDATES: 23 JUL 2006 HIGHEST RN 895579-80-3

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REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

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Uploading C:\Program Files\Stnexp\Queries\10736004a.str

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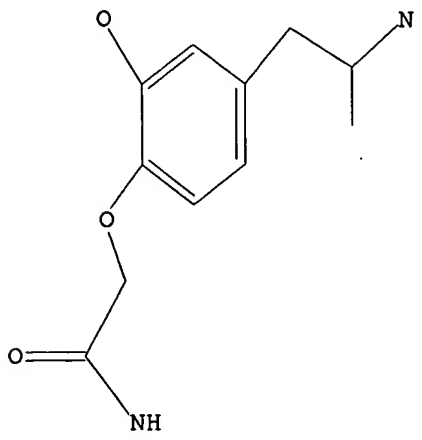
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SCREEN SEARCH COMPLETED - 26 TO ITERATE

100.0% PROCESSED 26 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 215 TO 825
PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

=> s l1 sss full
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FULL SCREEN SEARCH COMPLETED - 539 TO ITERATE

100.0% PROCESSED 539 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

L3 0 SEA SSS FUL L1

=>
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L4 STRUCTURE UPLOADED

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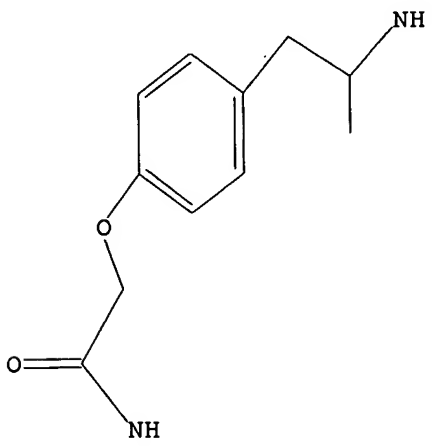
L4 HAS NO ANSWERS
L4 STR



Structure attributes must be viewed using STN Express query preparation.

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100.0% PROCESSED 191 ITERATIONS 18 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 2991 TO 4649
PROJECTED ANSWERS: 106 TO 614

L5 18 SEA SSS SAM L4

=>
Uploading C:\Program Files\Stnexp\Queries\10736004b.str

L6 STRUCTURE UPLOADED

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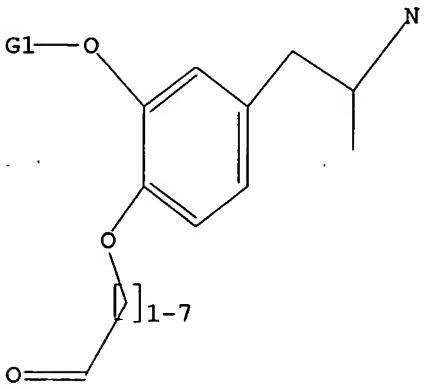
L6 HAS NO ANSWERS
L6 STR



G1 OH,Ak

Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SCREEN SEARCH COMPLETED - 60 TO ITERATE

100.0% PROCESSED 60 ITERATIONS 2 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 736 TO 1664
PROJECTED ANSWERS: 2 TO 124

L7 2 SEA SSS SAM L6

=> s l6 sss full
FULL SEARCH INITIATED 14:31:34 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 1301 TO ITERATE

100.0% PROCESSED 1301 ITERATIONS 35 ANSWERS
SEARCH TIME: 00.00.01

L8 35 SEA SSS FUL L6

```
=> FIL CAPLUS
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                       339.60     339.81

FILE 'CAPLUS' ENTERED AT 14:31:48 ON 25 JUL 2006
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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE COVERS 1907 - 25 Jul 2006  VOL 145 ISS 5
FILE LAST UPDATED: 24 Jul 2006  (20060724/ED)

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http://www.cas.org/infopolicy.html

=> s l8
L9          20 L8

=> s l9 and (carrier or label or BSA or ovalbumin or KHL)
        269716 CARRIER
        151068 CARRIERS
        353344 CARRIER
                  (CARRIER OR CARRIERS)
         61289 LABEL
         21123 LABELS
         73611 LABEL
                  (LABEL OR LABELS)
         15672 BSA
            77 BSAS
         15713 BSA
                  (BSA OR BSAS)
         14658 OVALBUMIN
          5697 OVALBUMINS
         16965 OVALBUMIN
                  (OVALBUMIN OR OVALBUMINS)
           250 KHL
             1 KHLS
           251 KHL
                  (KHL OR KHLS)
L10           2 L9 AND (CARRIER OR LABEL OR BSA OR OVALBUMIN OR KHL)

=> d l10 ibib abs hitstr tot

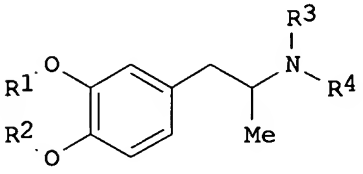
L10  ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2005:525102  CAPLUS
DOCUMENT NUMBER:          143:21369
TITLE:                    Assay for entactogens
INVENTOR(S):              Zheng, Yi Feng; Liu, Hshiou-Ting
```

PATENT ASSIGNEE(S): Dade Behring Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 44 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005130244	A1	20050616	US 2003-736005	20031215
US 6991911	B2	20060131		
WO 2005058864	A1	20050630	WO 2004-US41618	20041213

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-736005 A 20031215
OTHER SOURCE(S): MARPAT 143:21369
GI



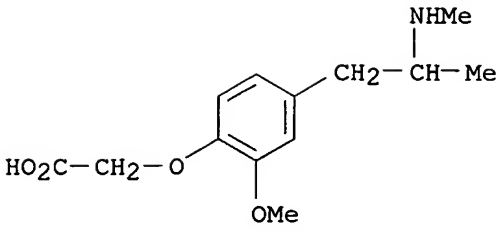
I

AB Methods, compns. and kits are disclosed. The methods are directed to determining the presence of entactogen analytes such as, for example, 3,4-methylenedioxyamphetamine (MDA), 3,4-methylenedioxy-methamphetamine (MDMA), 3,4-methylenedioxy-ethylamphetamine (MDEA) and 4-hydroxy-3-methoxy-methamphetamine (HMMA). The method comprises providing in combination in a medium (i) a sample suspected of containing the compound and (ii) an antibody raised against a compound of Formula I that comprises a protein. The medium is examined for the presence a complex comprising the compound and the antibody where the presence of such as complex indicates the presence of the compound in the sample. In one aspect of the above embodiment, the combination further comprises a label conjugate of the compound Formula I.

IT 853062-50-7DP, protein conjugates
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(method for detection of entactogens using antibodies and amphetamine analog-enzyme conjugates)

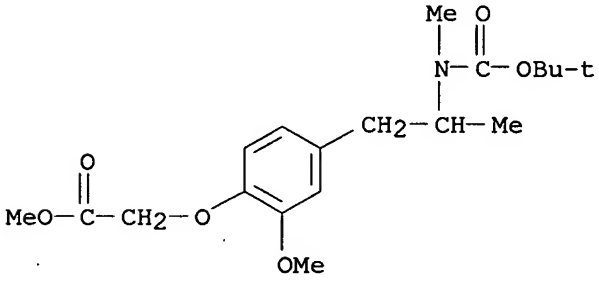
RN 853062-50-7 CAPLUS

CN Acetic acid, [2-methoxy-4-[2-(methylamino)propyl]phenoxy]- (9CI) (CA INDEX NAME)



IT 853062-41-6P 853062-44-9P 853062-46-1P
853062-48-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(method for detection of entactogens using antibodies and amphetamine analog-enzyme conjugates)

RN 853062-41-6 CAPLUS
CN Acetic acid, [4-[2-[[(1,1-dimethylethoxy)carbonyl]methylamino]propyl]-2-methoxyphenoxy]-, methyl ester (9CI) (CA INDEX NAME)



RN 853062-44-9 CAPLUS
CN Acetic acid, [2-methoxy-4-[2-(methylamino)propyl]phenoxy]-, methyl ester, trifluoroacetate (9CI) (CA INDEX NAME)

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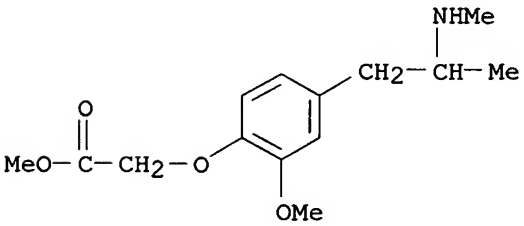
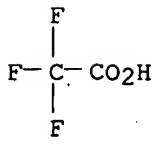
CRN 853062-43-8
CMF C14 H21 N O4



CM 2

CRN 76-05-1
CMF C2 H F3 O2



RN 853062-46-1 CAPLUS
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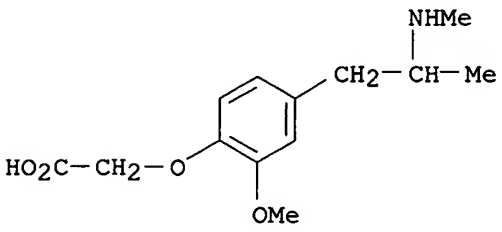
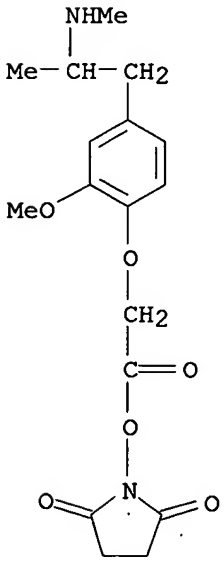


● HCl

RN 853062-48-3 CAPLUS
CN 2,5-Pyrrolidinedione, 1-[[[2-methoxy-4-[2-(methylamino)propyl]phenoxy]acetyl]oxy]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 87 THERE ARE 87 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:525101 CAPLUS
DOCUMENT NUMBER: 143:21368
TITLE: Assay for entactogens
INVENTOR(S): Zheng, Yi Feng; Liu, Hshiou-Ting; Yang, Yali
PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 39 pp.
CODEN: USXXCO

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

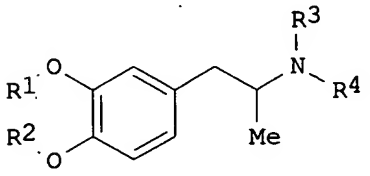
This application

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005130243	A1	20050616	US 2003-736004	20031215
WO 2005058865	A2	20050630	WO 2004-US41622	20041213
WO 2005058865	A3	20050804		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-736004 A 20031215
OTHER SOURCE(S): MARPAT 143:21368
GI



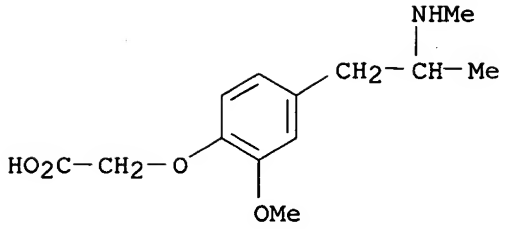
I

AB Methods, compns. and kits are disclosed. The methods are directed to determining the presence of entactogen analytes such as, for example, 3,4-methylenedioxyamphetamine (MDA), 3,4-methylenedioxymethamphetamine (MDMA), 3,4-methylenedioxyethylamphetamine (MDEA) and 4-hydroxy-3-methoxymethamphetamine (HMMA). The method comprises providing in combination in a medium (i) a sample suspected of containing the compound and (ii) an antibody raised against a compound of Formula I that comprises a protein. The medium is examined for the presence a complex comprising the compound and the antibody where the presence of such as complex indicates the presence of the compound in the sample. In one aspect of the above embodiment, the combination further comprises a label conjugate of the compound Formula I.

IT 853062-50-7DP, protein conjugates
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(method for detection of entactogens using antibodies and amphetamine analog-enzyme conjugates)

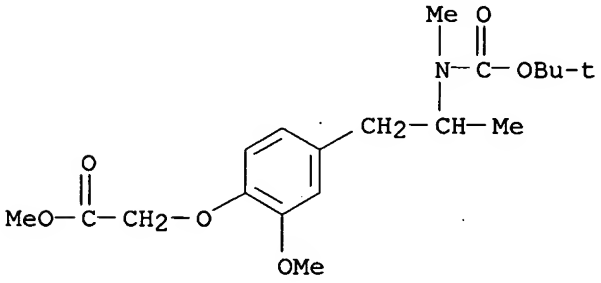
RN 853062-50-7 CAPLUS

CN Acetic acid, [2-methoxy-4-[2-(methylamino)propyl]phenoxy]- (9CI) (CA INDEX NAME)



IT 853062-41-6P 853062-44-9P 853062-46-1P
853062-48-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(method for detection of entactogens using antibodies and amphetamine analog-enzyme conjugates)

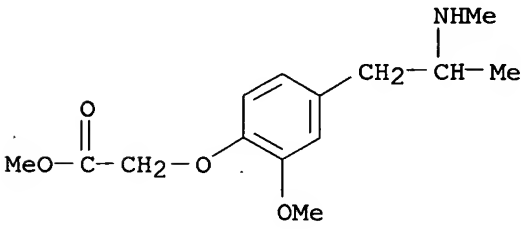
RN 853062-41-6 CAPLUS
CN Acetic acid, [4-[2-[[(1,1-dimethylethoxy)carbonyl]methylamino]propyl]-2-methoxyphenoxy]-, methyl ester (9CI) (CA INDEX NAME)



RN 853062-44-9 CAPLUS
CN Acetic acid, [2-methoxy-4-[2-(methylamino)propyl]phenoxy]-, methyl ester, trifluoroacetate (9CI) (CA INDEX NAME)

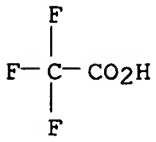
CM 1

CRN 853062-43-8
CMF C14 H21 N O4

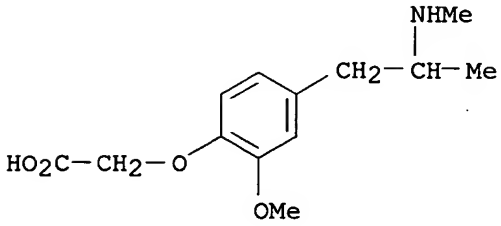


CM 2

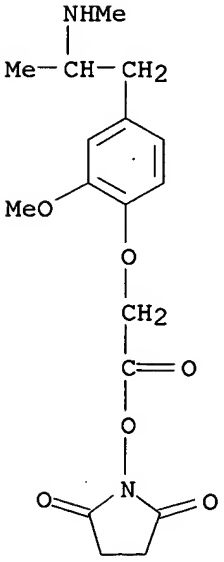
CRN 76-05-1
CMF C2 H F3 O2



RN 853062-46-1 CAPLUS
CN Acetic acid, [2-methoxy-4-[2-(methylamino)propyl]phenoxy]-, hydrochloride (9CI) (CA INDEX NAME)



RN 853062-48-3 CAPLUS
CN 2,5-Pyrrolidinedione, 1-[[[2-methoxy-4-[2-(methylamino)propyl]phenoxy]acetyl]oxy]- (9CI) (CA INDEX NAME)



=> s l9 not l10
L11 18 L9 NOT L10

=> d l11 ibib abs hitstr tot

L11 ANSWER 1 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:569849 CAPLUS

DOCUMENT NUMBER: 141:89372
TITLE: Preparation of tripeptides as inhibitors of the Yersinia phosphatase (YopH) enzyme
INVENTOR(S): Burke, Terrence R.; Lee, Kyeong; Gao, Yang; Phan, Jason; Waugh, David S.
PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA
SOURCE: U.S. Pat. Appl. Publ., 15 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004138104	A1	20040715	US 2003-341607	20030114
WO 2004065411	A2	20040805	WO 2004-US669	20040112
WO 2004065411	A3	20050127		

W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI

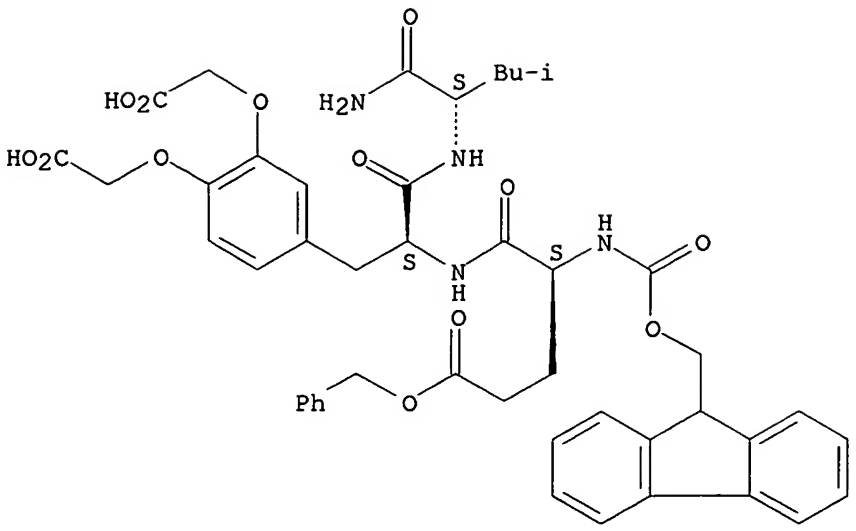
PRIORITY APPLN. INFO.: US 2003-341607 A 20030114
OTHER SOURCE(S): MARPAT 141:89372

AB Disclosed are tripeptides of formula P-A-B-C [A is an amino acid having a carboxyalkyl group, B is (un)substituted tyrosine or phenylalanine, C is a hydrophobic amino acid, and P is an amine protecting group (with provisos)] or their prodrugs for use in pharmaceutical compns. for treating an animal, e.g., a human, exposed to or infected by Yersinia pestis. The compds. find use as anti-bioterrorism agents. Tripeptides of the invention were prepared by the Fmoc-based solid-phase method. Fmoc-L-Glu-L-Tyr(CH2CO2H)-L-Leu-NH2 showed IC50 values 4.6 ± 2 and 2.8 ± 1.1μM for inhibition of protein tyrosine phosphatase 1B (PTB1B) and YopH, resp.

IT 596814-15-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of tripeptides as inhibitors of Yersinia phosphatase (YopH) enzyme for use as anti-bioterrorism agents)

RN 596814-15-2 CAPLUS
CN L-Leucinamide, N-[(9H-fluoren-9-ylmethoxy)carbonyl]-L-α-glutamyl-3-(carboxymethoxy)-O-(carboxymethyl)-L-tyrosyl-, 1-(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

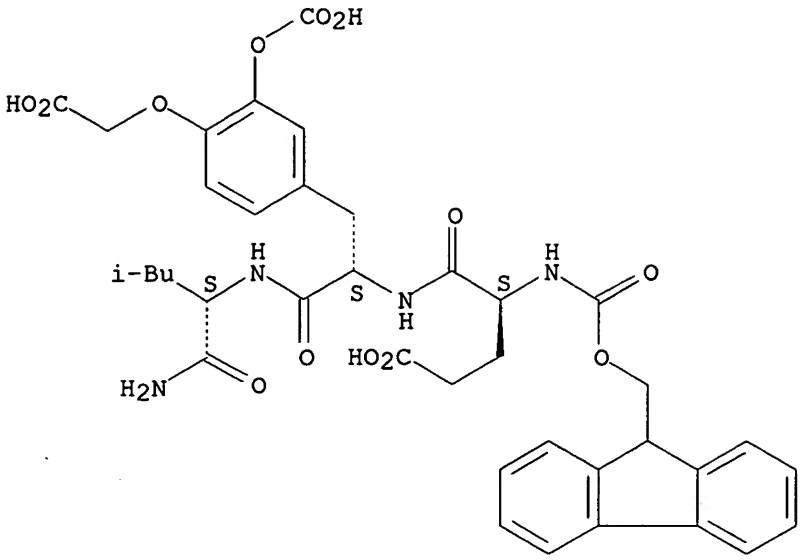


L11 ANSWER 2 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:243068 CAPLUS
DOCUMENT NUMBER: 141:3192
TITLE: Phosphotyrosyl peptides and analogues as substrates and inhibitors of purple acid phosphatases
AUTHOR(S): Valizadeh, Mohsen; Schenk, Gerhard; Nash, Kevin; Oddie, Geoff W.; Guddat, Luke W.; Hume, David A.; de Jersey, John; Burke, Terrence R.; Hamilton, Susan
CORPORATE SOURCE: Department of Biochemistry, The University of Queensland, St. Lucia, 4072, Australia
SOURCE: Archives of Biochemistry and Biophysics (2004), 424(2), 154-162
CODEN: ABBIA4; ISSN: 0003-9861
PUBLISHER: Elsevier Science
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Purple acid phosphatases are metal-containing hydrolases. While their precise biol. role(s) is unknown, the mammalian enzyme has been linked in a variety of biol. circumstances (e.g., osteoporosis) with increased bone resorption. Inhibition of the human enzyme is a possible strategy for the treatment of bone-resorptive diseases such as osteoporosis. Previously, we determined the crystal structure of pig purple acid phosphatase to 1.55 A and we showed that it is a good model for the human enzyme. Here, a study of the pH dependence of its kinetic parameters showed that the pig enzyme is most efficient at pH values similar to those encountered in the osteoclast resorptive space. Based on the observation that phosphotyrosine-containing peptides are good substrates for pig purple acid phosphatase, peptides containing a range of phosphotyrosine mimetics were synthesized. Kinetic anal. showed that they act as potent inhibitors of mammalian and plant purple acid phosphatases, with the best inhibitors exhibiting low micromolar inhibition consts. at pH 3-5. These compds. are thus the most potent organic inhibitors yet reported for the purple acid phosphatases.

IT 697287-29-9
RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitor, kinetics; phosphotyrosyl peptides and analogs as substrates and inhibitors of plant and mammalian purple acid phosphatases)
RN 697287-29-9 CAPLUS
CN L-Leucinamide, N-[(9H-fluoren-9-ylmethoxy)carbonyl]-L-α-glutamyl-O-(carboxymethyl)-3-(carboxyoxy)-L-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

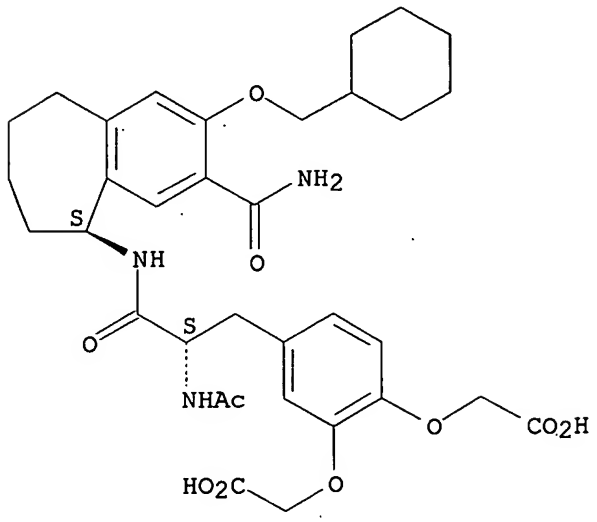
L11 ANSWER 3 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:209677 CAPLUS
DOCUMENT NUMBER: 140:417241
TITLE: Structure-based design of novel nonpeptide inhibitors of the Src SH2 domain: phosphotyrosine mimetics exploiting multifunctional group replacement chemistry
AUTHOR(S): Sundaramoorthi, Raji; Kawahata, Noriyuki; Yang, Michael G.; Shakespeare, William C.; Metcalf, Chester A., III; Wang, Yihan; Merry, Taylor; Eyermann, Charles J.; Bohacek, Regine S.; Narula, Surinder; Dalgarno, David C.; Sawyer, Tomi K.
CORPORATE SOURCE: ARIAD Pharmaceuticals, Cambridge, MA, 02139-4234, USA
SOURCE: Biopolymers (2003), 71(6), 717-729
CODEN: BIPMAA; ISSN: 0006-3525
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A series of novel nonpeptide inhibitors of the pp60c-Src (Src) SH2 domain is described that exploit multifunctional group replacement of the phenylphosphate moiety of phosphotyrosine (pTyr). Relative to an x-ray structure of citrate complexed to the pTyr binding site of the Src SH2 domain, these nonpeptide ligands illustrate the systematic replacement of the phosphate group by multiple nonhydrolyzable, mono- or dianionic functionalities. Specifically, several phenylalanine (Phe) analogs incorporating key 4' and 3' substituents were synthesized and incorporated into a bicyclic benzamide template previously reported. These pTyr mimetics included 4',3'-diphosphono-Phe (Dpp), 4',3'-dicarboxymethyloxy-Phe (Dcp), and 4'-phosphono-3'-carboxymethyloxy-Phe (Cpp). Noteworthy were nonpeptide inhibitors 8-11 that were 5- to 10-fold more potent than the cognate tetrapeptide ligand Ac-pTyr-Glu-Glu-Ile-NH2 in binding to the Src SH2 domain.

IT 268741-58-8
RL: PAC (Pharmacological activity); BIOL (Biological study)
(structure-based design of novel nonpeptide inhibitors of the Src SH2 domain)
RN 268741-58-8 CAPLUS

CN Acetic acid, 2,2'-[[4-[(2S)-2-(acetylamino)-3-[[(5S)-3-(aminocarbonyl)-2-(cyclohexylmethoxy)-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-yl]amino]-3-oxopropyl]-1,2-phenylene]bis(oxy)]bis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 4 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:521345 CAPLUS
DOCUMENT NUMBER: 139:239667
TITLE: Tripeptide inhibitors of Yersinia protein-tyrosine phosphatase
AUTHOR(S): Lee, Kyeong; Gao, Yang; Yao, Zhu-Jun; Phan, Jason; Wu, Li; Liang, Jiao; Waugh, David S.; Zhang, Zhong-Yin; Burke, Terrence R.
CORPORATE SOURCE: CCR, Laboratory of Medicinal Chemistry, NIH,, NCI-Frederick, Frederick, MD, 21702, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2003), 13(15), 2577-2581
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The protein-tyrosine phosphatase (PTP) YopH' is a virulence factor of Yersinia pestis, the causative agent of plague. Potential use of Yersinia as a bioterrorism agent renders YopH inhibitors of therapeutic importance. Previously, we had examined the inhibitory potencies of a variety of phosphotyrosyl (pTyr) mimetics against the human PTP1B enzyme by displaying them in the EGFR-derived hexapeptide sequence,Ac-Asp-Ala-Asp-Glu-Xxx-Leu-amide', where Xxx=pTyr mimetic. The poor inhibitory potencies of certain of these pTyr mimetics were attributed to restricted orientation within the PTP1B catalytic pocket incurred by extensive peripheral interaction of the hexapeptide platform. Utilizing the smaller tripeptide platform, Fmoc-Glu-Xxx-Leu-amide' we demonstrate herein that several of the low affinity hexapeptide-expressed pTyr mimetics exhibit high PTP1B affinity within the context of the tripeptide platform. Of particular note, the mono-anionic 4-(carboxydifluoromethyl)Phe residue exhibits affinity equivalent to the di-anionic F2Pmp residue, which had previously been among the most potent PTP-binding motifs. Against YopH, it was found that all tripeptides having Glu residues with an unprotected

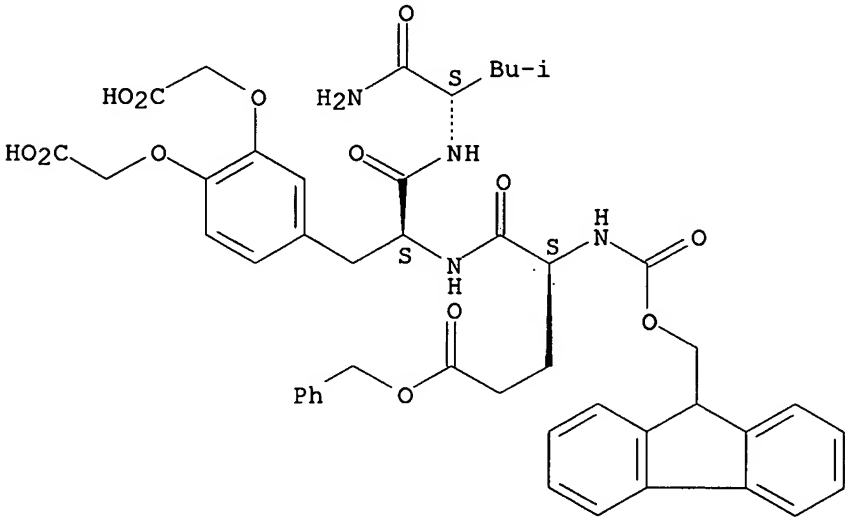
side chain carboxyl were inactive. Alternatively, in their Glu-OBn ester forms, several of the tripeptides exhibited good YopH affinity with the mono-anionic peptide, Fmoc-Glu(OBn)-Xxx-Leu-amide, where Xxx=4-(carboxymethyloxy)Phe providing an IC50 value of 2.8 μM. One concern with such inhibitors is that they may potentially function by non-specific mechanisms. Studies with representative inhibitors, while failing to provide evidence of a non-specific promiscuous mode of inhibition, did indicate that non-classical inhibition may be involved.

IT 596814-15-2
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(structure-activity relationship of tripeptide inhibitors of Yersinia protein-tyrosine phosphatase)

RN 596814-15-2 CAPLUS

CN L-Leucinamide, N-[(9H-fluoren-9-ylmethoxy)carbonyl]-L-α-glutamyl-3-(carboxymethoxy)-O-(carboxymethyl)-L-tyrosyl-, 1-(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 5 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:484863 CAPLUS

DOCUMENT NUMBER: 137:47448

TITLE: Preparation of substituted phenylalaninol derivatives as protein tyrosine phosphatase inhibitors

INVENTOR(S): Larsen, Scott D.; May, Paul D.; Bleasdale, John E.; Liljebris, Charlotta; Schostarez, Heinrich Josef; Barf, Tjeerd; Nilsson, Marianne

PATENT ASSIGNEE(S): USA

SOURCE: U.S., 144 pp., Cont.-in-part of U.S. Ser. No. 138,642.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6410585	B1	20020625	US 1999-265410	19990310

US 6353023	B1	20020305	US 1998-138642		19980824
CA 2366308	AA	20000914	CA 2000-2366308		20000309
WO 2000053583	A1	20000914	WO 2000-US6022		20000309
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
EP 1161421	A1	20011212	EP 2000-917793		20000309
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
JP 2002539115	T2	20021119	JP 2000-604023		20000309
AU 769511	B2	20040129	AU 2000-38711		20000309
PRIORITY APPLN. INFO.:			US 1997-57730P	P	19970828
			US 1998-138642	A2	19980824
			US 1999-265410	A	19990310
			WO 2000-US6022	W	20000309

OTHER SOURCE(S): MARPAT 137:47448

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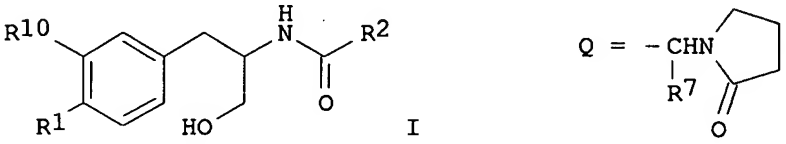


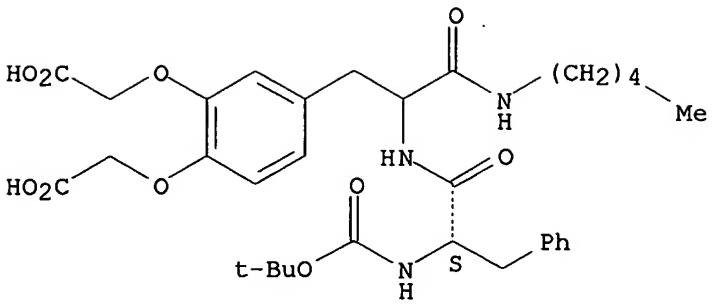
AB The invention comprises phenylalaninol derivs., e.g., I [R1 = OSO3H, OCH(CO2R5)2, OCH2CO2R5, OCH(CO2R5)CH2CO2R5, OC(CO2R5):CHCO2R5, CH2CH(CO2R5)2, CH:C(CO2R5)2, OCH2CONHOH, N(CH2CO2R5)2, OCHFCO2R5 (R5 = H, alkyl, alkylphenyl); R2 = CHR7NHXR6, group Q (R6 = alkyl, alkyl-CONH2, alkyl-NHCO2R5, etc.; R7 = H, any group given for R6); R10 = H, CO2R5, CONHOH, 5-tetrazolyl, F, OCH2CO2R5], or their pharmaceutically acceptable salts, as small mol. weight, non-peptidic inhibitors of protein tyrosine phosphatase 1 (PTP1) which are useful for the treatment and/or prevention of non-insulin dependent diabetes mellitus. Thus, 5-[(2S)-2-[[(2S)-2-[(tert-butoxycarbonyl)amino]-3-phenylpropanoyl]amino]-3-hydroxypropyl]-2-(carboxymethoxy)benzoic acid (claimed compound) was prepared and showed 80% inhibition of protein tyrosine phosphatase 1B at a concentration of 10 μM.

IT 221076-92-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted phenylalanine derivs. as protein tyrosine phosphatase inhibitors)

RN 221076-92-2 CAPLUS

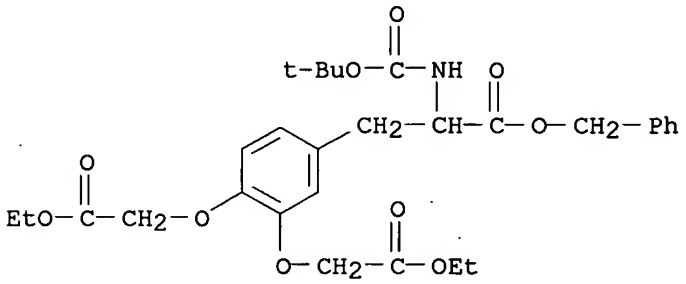
CN Tyrosinamide, N-[(1,1-dimethylethoxy)carbonyl]-L-phenylalanyl-3-(carboxymethoxy)-O-(carboxymethyl)-N-pentyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

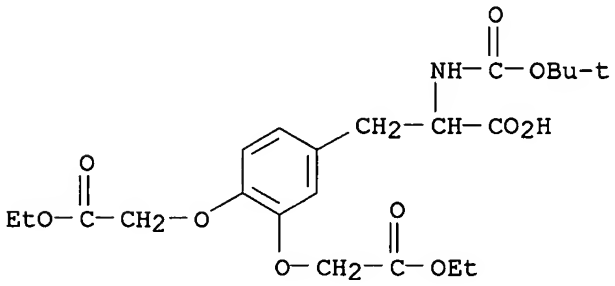


IT 221077-95-8P 221077-97-0P 221077-98-1P
221077-99-2P 221078-02-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of substituted phenylalanine derivs. as protein tyrosine phosphatase inhibitors)

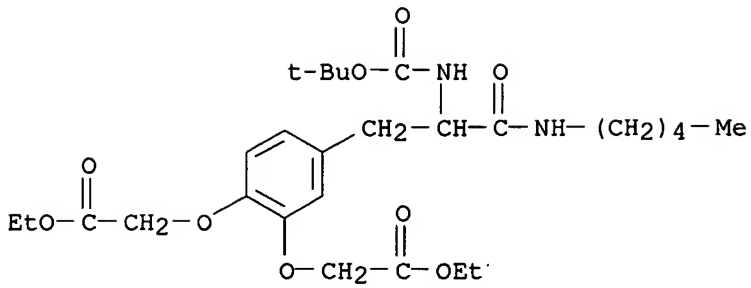
RN 221077-95-8 CAPLUS
CN Tyrosine, N-[(1,1-dimethylethoxy)carbonyl]-3-(2-ethoxy-2-oxoethoxy)-O-(2-ethoxy-2-oxoethyl)-, phenylmethyl ester (9CI) (CA INDEX NAME)



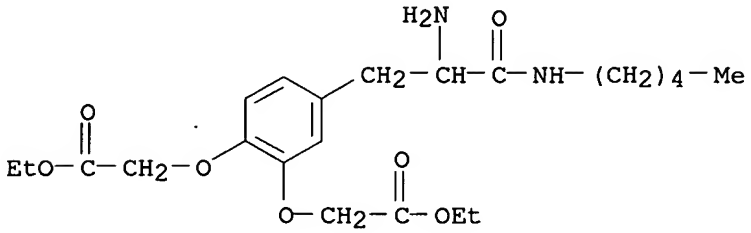
RN 221077-97-0 CAPLUS
CN Tyrosine, N-[(1,1-dimethylethoxy)carbonyl]-3-(2-ethoxy-2-oxoethoxy)-O-(2-ethoxy-2-oxoethyl)- (9CI) (CA INDEX NAME)



RN 221077-98-1 CAPLUS
CN Acetic acid, 2,2'-[[4-[2-[[(1,1-dimethylethoxy)carbonyl]amino]-3-oxo-3-(pentylamino)propyl]-1,2-phenylene]bis(oxy)]bis-, diethyl ester (9CI) (CA INDEX NAME)

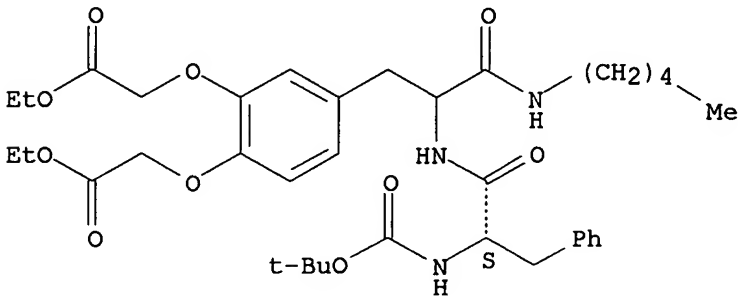


RN 221077-99-2 CAPLUS
CN Acetic acid, 2,2'-[[4-[2-amino-3-oxo-3-(pentylamino)propyl]-1,2-phenylene]bis(oxy)]bis-, diethyl ester (9CI) (CA INDEX NAME)



RN 221078-02-0 CAPLUS
CN Tyrosinamide, N-[(1,1-dimethylethoxy)carbonyl]-L-phenylalanyl-3-(2-ethoxy-2-oxoethoxy)-O-(2-ethoxy-2-oxoethyl)-N-pentyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 6 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:772172 CAPLUS
DOCUMENT NUMBER: 135:331675
TITLE: Preparation of acylated oligopeptide derivatives having cell signal inhibiting activity
INVENTOR(S): Burke, Terrence R., Jr.; Yao, Zhu-Jun; King, C. Richter
PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA
SOURCE: U.S., 42 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6307090	B1	20011023	US 1999-236160	19990122
PRIORITY APPLN. INFO.:			US 1999-236160	19990122
OTHER SOURCE(S):	MARPAT 135:331675			

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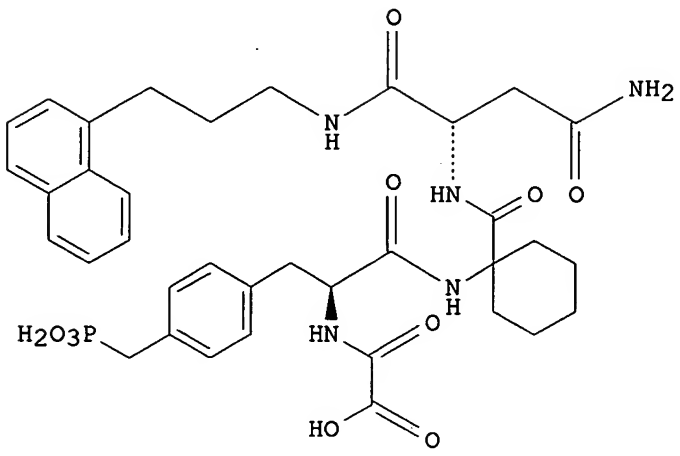


I

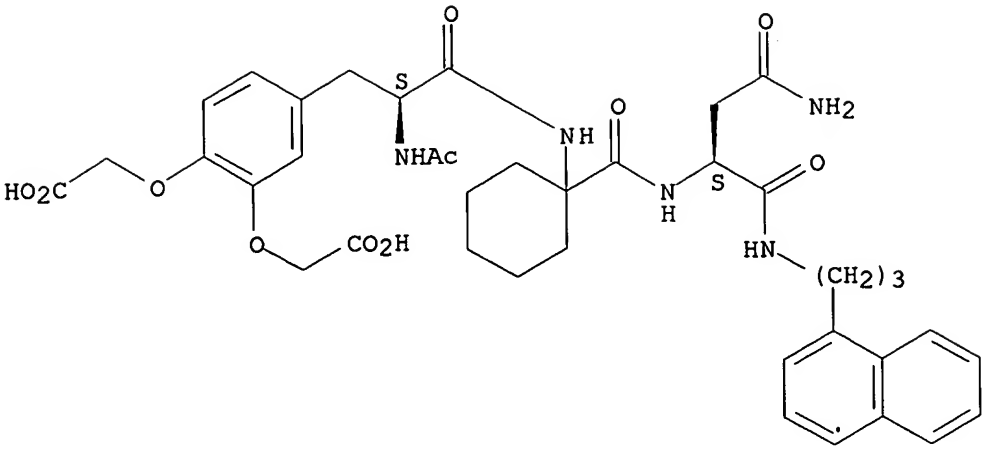
AB The invention relates to acylated peptides X-PTI-(AA)n-Y (n = 0-15; X is oxalyl; PTI is a bivalent radical of phosphotyrosine or of an amino acid selected from the group consisting of phosphonomethylphenylalanine, phosphono(α-fluoro or α,α-difluoro)methylphenylalanine, phosphono(α-hydroxy)methylphenylalanine, O-sulfotyrosine, phosphonophenylalanine, dicarboxymethoxyphenylalanine, aspartic acid, glutamic acid, phosphoserine and phosphothreonine, each of which is present in the DL-, D- or L-form; AA is a bivalent radical of a natural or unnatural amino acid; Y is secondary amino group) or their salts, which are useful for the treatment of diseases that respond to inhibition of the interaction of a protein comprising an SH2 domain and a protein tyrosine kinase or a modified version. Several peptides, e.g, I, were prepared by a multistep procedure and their Grb2 SH2 domain binding affinities are shown graphically.

IT 220193-79-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of acylated oligopeptide derivs. having cell signal inhibiting activity)

RN 220193-79-3 CAPLUS

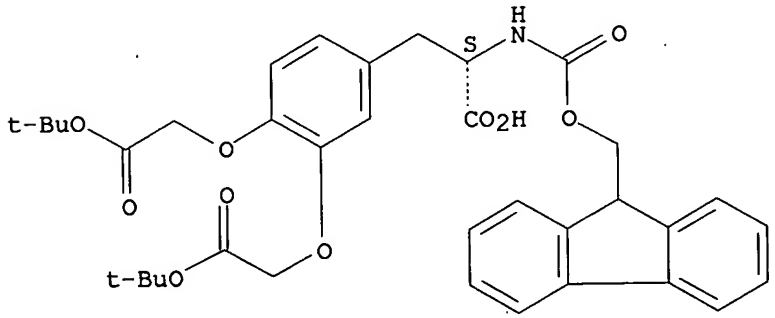
CN L-Aspartamide, N-acetyl-3-(carboxymethoxy)-O-(carboxymethyl)-L-tyrosyl-1-aminocyclohexanecarbonyl-N1-[3-(1-naphthalenyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



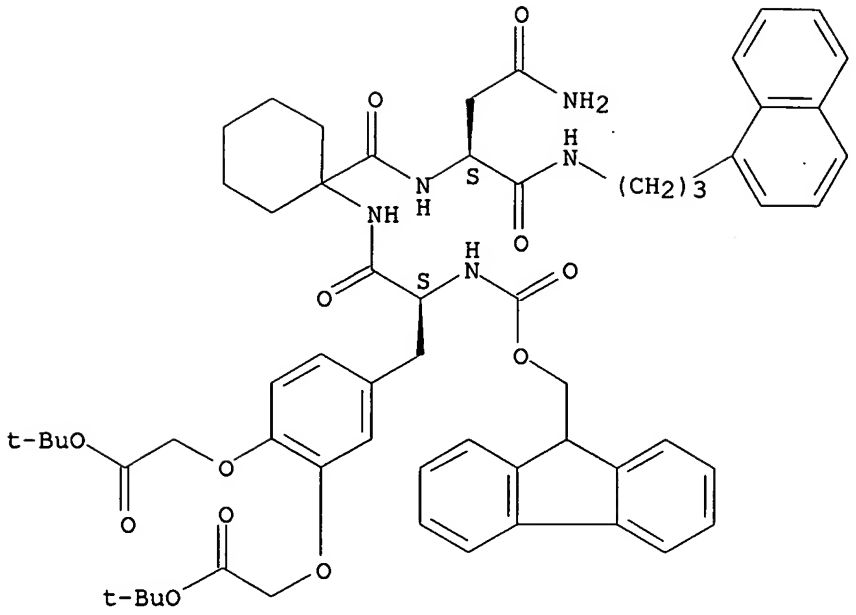
IT 213757-63-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of acylated oligopeptide derivs. having cell signal inhibiting activity)
RN 213757-63-2 CAPLUS
CN L-Tyrosine, 3-[2-(1,1-dimethylethoxy)-2-oxoethoxy]-O-[2-(1,1-dimethylethoxy)-2-oxoethyl]-N-[(9H-fluoren-9-ylmethoxy)carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



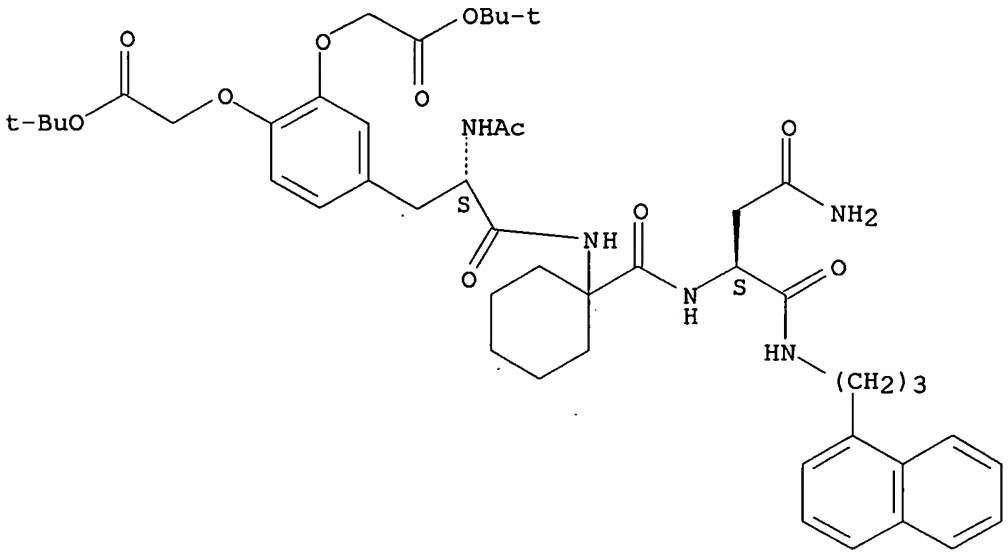
IT 220193-62-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of acylated oligopeptide derivs. having cell signal inhibiting activity)
RN 220193-62-4 CAPLUS
CN L-Aspartamide, 3-[2-(1,1-dimethylethoxy)-2-oxoethoxy]-O-[2-(1,1-dimethylethoxy)-2-oxoethyl]-N-[(9H-fluoren-9-ylmethoxy)carbonyl]-L-phenylalanyl-1-aminocyclohexanecarbonyl-N1-[3-(1-naphthalenyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 220193-73-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of acylated oligopeptide derivs. having cell signal inhibiting activity)
RN 220193-73-7 CAPLUS
CN L-Aspartamide, N-acetyl-3-[2-(1,1-dimethylethoxy)-2-oxoethoxy]-O-[2-(1,1-dimethylethoxy)-2-oxoethyl]-L-tyrosyl-1-aminocyclohexanecarbonyl-N1-[3-(1-naphthalenyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 113 THERE ARE 113 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 7 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:329848 CAPLUS
DOCUMENT NUMBER: 135:29429

TITLE: Potent blockade of hepatocyte growth factor-stimulated cell motility, matrix invasion and branching morphogenesis by antagonists of Grb2 Src homology 2 domain interactions

AUTHOR(S): Atabey, Nese; Gao, Yang; Yao, Zhu-Jun; Breckenridge, Diane; Soon, Lilian; Soriano, Jesus V.; Burke, Terrence R., Jr.; Bottaro, Donald P.

CORPORATE SOURCE: Laboratories of Cellular and Molecular Biology, Division of Basic Sciences, NCI, National Institutes of Health, Bethesda, MD, 20892-4255, USA

SOURCE: Journal of Biological Chemistry (2001), 276(17), 14308-14314
CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

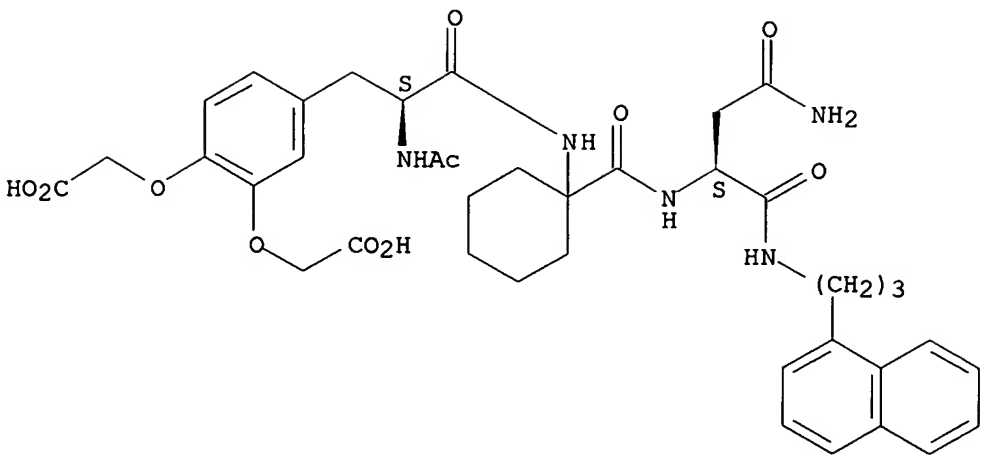
AB Hepatocyte growth factor (HGF) stimulates mitogenesis, motogenesis, and morphogenesis in a wide range of cellular targets during development, homeostasis and tissue regeneration. Inappropriate HGF signaling occurs in several human cancers, and the ability of HGF to initiate a program of protease production, cell dissociation, and motility has been shown to promote cellular invasion and is strongly linked to tumor metastasis. Upon HGF binding, several tyrosines within the intracellular domain of its receptor, c-Met, become phosphorylated and mediate the binding of effector proteins, such as Grb2. Grb2 binding through its SH2 domain is thought to link c-Met with downstream mediators of cell proliferation, shape change, and motility. We analyzed the effects of Grb2 SH2 domain antagonists on HGF signaling and observed potent blockade of cell motility, matrix invasion, and branching morphogenesis, with ED50 values of 30 nM or less, but only modest inhibition of mitogenesis. These compds. are 1000-10,000-fold more potent anti-motility agents than any previously characterized Grb2 SH2 domain antagonists. Our results suggest that SH2 domain-mediated c-Met-Grb2 interaction contributes primarily to the motogenic and morphogenic responses to HGF, and that these compds. may have therapeutic application as anti-metastatic agents for tumors where the HGF signaling pathway is active.

IT 220193-79-3
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(HGF-stimulated cell motility and matrix invasion and branching morphogenesis potent blockade by antagonists of Grb2 Src homol. 2 domain interactions)

RN 220193-79-3 CAPLUS

CN L-Aspartamide, N-acetyl-3-(carboxymethoxy)-O-(carboxymethyl)-L-tyrosyl-1-aminocyclohexanecarbonyl-N1-[3-(1-naphthalenyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 8 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:300535 CAPLUS
DOCUMENT NUMBER: 134:320849
TITLE: Peptides for inhibition of cell motility and angiogenesis
INVENTOR(S): Bottaro, Donald P.; Atabey, Safiye N.; Soriano, Jesus V.; Breckenridge, Diane E.; Yao, Zhu-jun; Gao, Yang
PATENT ASSIGNEE(S): The Government of the United States of America, Represented by the Secretary, Department of Health and Human Services, USA; Burke, Terrence R., Jr.
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001028577	A2	20010426	WO 2000-US41423	20001020
WO 2001028577	A3	20011213		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2387922	AA	20010426	CA 2000-2387922	20001020
AU 2001029166	A5	20010430	AU 2001-29166	20001020
AU 780697	B2	20050414		
EP 1223959	A2	20020724	EP 2000-992431	20001020
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003512334	T2	20030402	JP 2001-531405	20001020

PRIORITY APPLN. INFO.:	US 1999-160899P	P	19991022
	US 2000-221525P	P	20000728
	WO 2000-US41423	W	20001020

OTHER SOURCE(S): MARPAT 134:320849

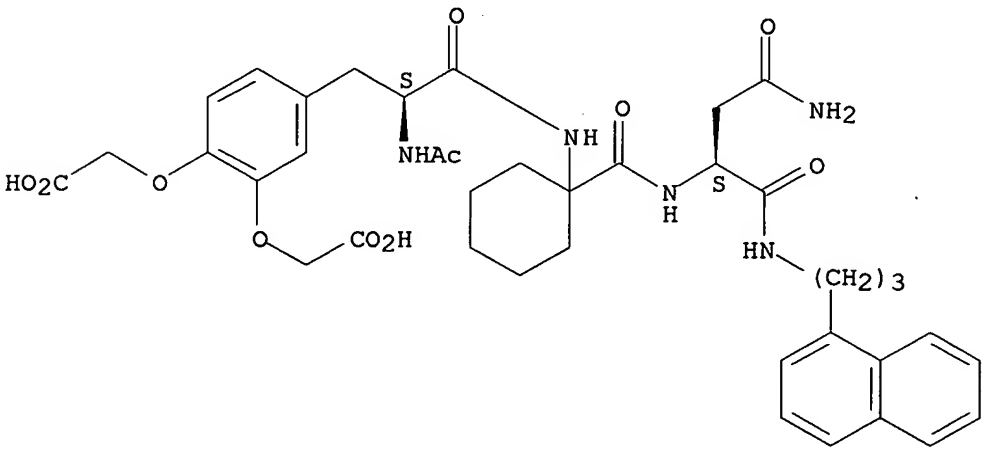
AB Disclosed are methods of inhibiting cell motility, for example, by inhibiting the binding between an intracellular transducer and a receptor protein tyrosine kinase, and more particularly by inhibiting hepatocyte growth factor (HGF)-induced cell motility. The present invention also provides a method of inhibiting angiogenesis. The methods of the present invention employ peptides such as phosphotyrosyl mimetics. The present invention further provides methods of preventing and/or treating diseases, disorders, states, or conditions such as cancer, particularly metastatic cancer comprising administering to a mammal of interest one or more peptides of the present invention. Also disclosed are methods of blocking HGF, VEGF, or bFGF-stimulated migration, cell proliferation, and formation of capillary-like structures. Addition of Grb2 inhibitor peptide 2 (30 nM, 300 nM) resulted in a significant, albeit markedly different, inhibition of proliferation in HUVE and HMVE cells.

IT 220193-79-3
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(control peptide; peptides for inhibition of cell motility and angiogenesis)

RN 220193-79-3 CAPLUS

CN L-Aspartamide, N-acetyl-3-(carboxymethoxy)-O-(carboxymethyl)-L-tyrosyl-1-aminocyclohexanecarbonyl-N1-[3-(1-naphthalenyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 9 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:894752 CAPLUS

DOCUMENT NUMBER: 135:70625

TITLE: Nonpeptide inhibitors of the pp60c-src (Src) SH2 domain: discovery of a novel phosphotyrosine mimetic

AUTHOR(S): Kawahata, Noriyuki; Yang, Michael; Luke, George; Shakespeare, William; Sundaramoorthi, Raji; Wang, Yihan; Johnson, Daniel; Merry, Taylor; Violette, Shelia; Guan, Wei; Bartlett, Catherine; Smith, Jeremy; Hatada, Marcos; Lu, Xiaode; Eyermann, Charles; Bohacek, Regine; Dalgarno, David; Sawyer, Tomi

CORPORATE SOURCE: ARIAD Pharmaceuticals, Inc., Cambridge, MA, 02139, USA

SOURCE: Peptides for the New Millennium, Proceedings of the American Peptide Symposium, 16th, Minneapolis, MN, United States, June 26-July 1, 1999 (2000), Meeting Date 1999, 561-562. Editor(s): Fields, Gregg B.; Tam,

James P.; Barany, George. Kluwer Academic Publishers: Dordrecht, Neth.
CODEN: 69ATHX
DOCUMENT TYPE: Conference
LANGUAGE: English

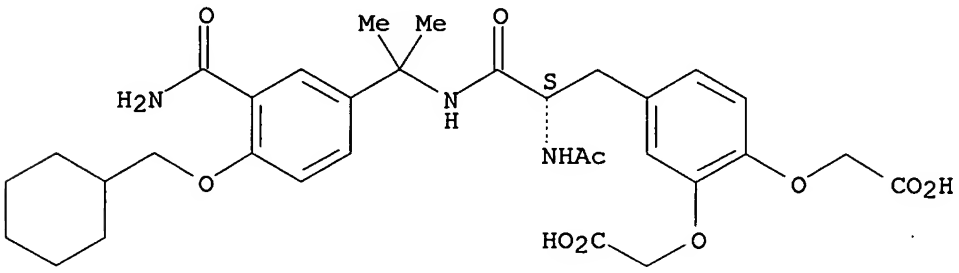
AB The observation that osteoporosis is the major phenotype in pp60SrC (Src) -/- mice highlights the potential of Src inhibition for the treatment of osteoporosis. Efforts to advance the discovery of a promising new class of anti-resorptive agents through the design, synthesis and incorporation of a novel phosphotyrosine mimetic, are hereby described.

IT 346717-49-5
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(nonpeptide inhibitors of pp60c-src SH2 domain)

RN 346717-49-5 CAPLUS

CN Acetic acid, 2,2'-[[4-[(2S)-2-(acetylamino)-3-[[1-[3-(aminocarbonyl)-4-(cyclohexylmethoxy)phenyl]-1-methylethyl]amino]-3-oxopropyl]-1,2-phenylene]bis(oxy)]bis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 10 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:380070 CAPLUS
DOCUMENT NUMBER: 133:187602
TITLE: Examination of novel non-phosphorus-containing phosphotyrosyl mimetics against protein-tyrosine phosphatase-1B and demonstration of differential affinities toward Grb2 SH2 domains
AUTHOR(S): Gao, Yang; Wu, Li; Luo, Juliet H.; Guo, Ribo; Yang, Dajun; Zhang, Zhong-Yin; Burke, Terrence R., Jr.
CORPORATE SOURCE: Laboratory of Medicinal Chemistry, Division of Basic Sciences, National Cancer Institute, National Institutes of Health, Bethesda, MD, 20892, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2000), 10(9), 923-927
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Inhibitory potencies were compared of several mono- and dicarboxy-based pTyr mimetics in Grb2 SH2 domain vs. protein-tyrosine phosphatase-1B (PTP1B) assays. Although in both systems pTyr residues provide critical binding elements, significant differences in the manner of recognition exist between the two. This is reflected in the current study, where marked variation in relative potencies was observed between the two systems. Of particular note was the poor potency of all monocarboxy-based pTyr mimetics against PTP1B when incorporated into a hexapeptide platform. The

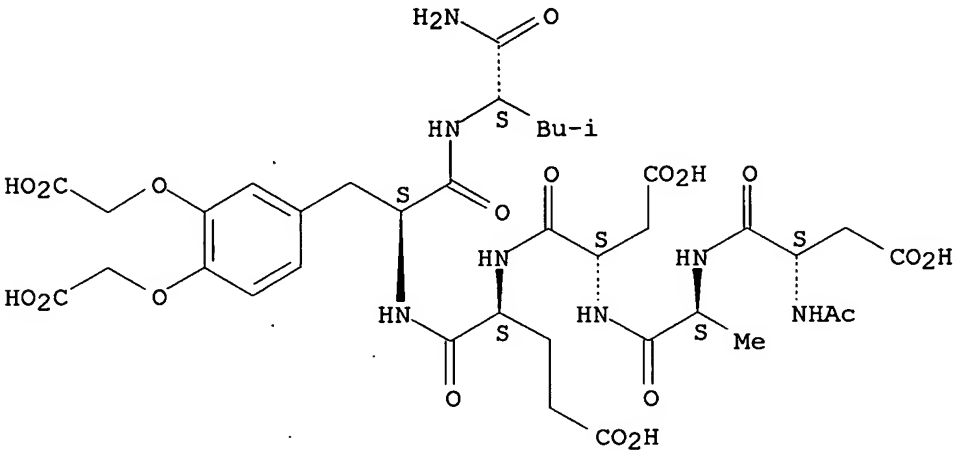
recently reported high PTP1B inhibitory potency of similar phenylphosphate mimicking moieties displayed in small mol., non-peptide structures, raises questions on the limitations of using peptides as platforms for pTyr mimetics in the discovery of small mol. inhibitors.

IT 213757-74-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(examination of novel non-phosphorus-containing phosphotyrosyl mimetics against protein-tyrosine phosphatase-1B and demonstration of differential affinities toward Grb2 SH2 domains)

RN 213757-74-5 CAPLUS

CN L-Leucinamide, N-acetyl-L-α-aspartyl-L-alanyl-L-α-aspartyl-L-α-glutamyl-3-(carboxymethoxy)-O-(carboxymethyl)-L-tyrosyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

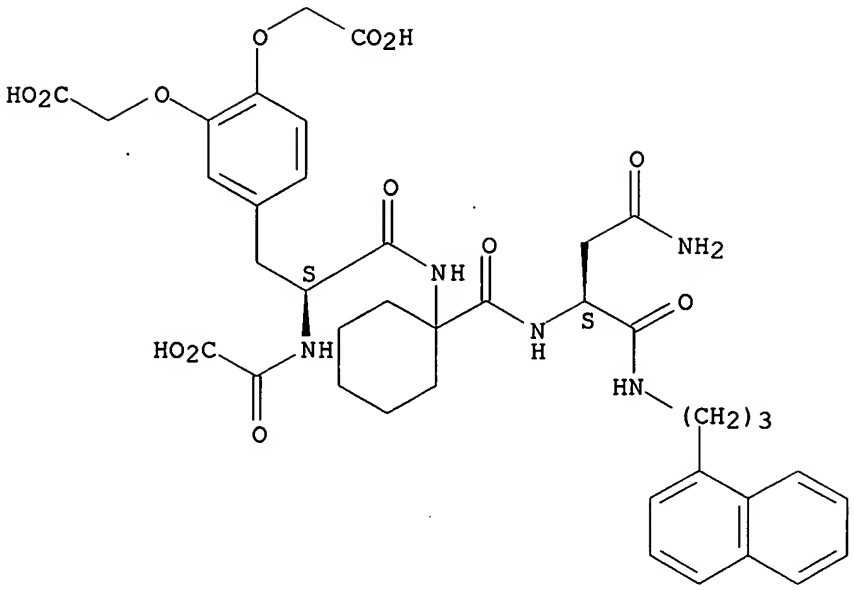


IT 288854-19-3
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(examination of novel non-phosphorus-containing phosphotyrosyl mimetics against protein-tyrosine phosphatase-1B and demonstration of differential affinities toward Grb2 SH2 domains)

RN 288854-19-3 CAPLUS

CN L-Aspartamide, N-(carboxycarbonyl)-3-(carboxymethoxy)-O-(carboxymethyl)-L-tyrosyl-1-aminocyclohexanecarbonyl-N1-[3-(1-naphthalenyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

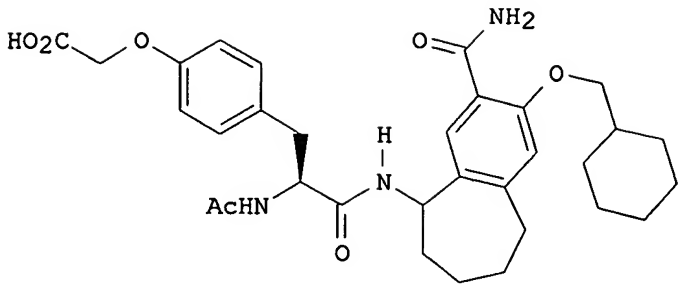


REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 11 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:335373 CAPLUS
DOCUMENT NUMBER: 132:347940
TITLE: Preparation of N-benzocycloheptenyl-L-tyrosinamides and analogs as intracellular signal transduction inhibitors
INVENTOR(S): Shakespeare, William C.; Yang, Michael G.; Sundaramoorthi, Rajeswari; Bohacek, Regine; Eyermann, Charles Joseph; Sawyer, Tomi K.
PATENT ASSIGNEE(S): Ariad Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 87 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2000027802	A1	20000518	WO 1999-US26986		19991112
W: CA, JP, US					
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
CA 2345459	AA	20000518	CA 1999-2345459		19991112
EP 1129068	A1	20010905	EP 1999-962770		19991112
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
JP 2002529444	T2	20020910	JP 2000-580982		19991112
US 2002137941	A1	20020926	US 2001-854027		20010511
US 6482852	B2	20021119			
US 2002062031	A1	20020523	US 2001-990637		20011121
US 6573295	B2	20030603			
PRIORITY APPLN. INFO.:			US 1998-108106P	P	19981112
			US 1999-438601	B3	19991112
			WO 1999-US26986	W	19991112

OTHER SOURCE(S): MARPAT 132:347940
GI



I

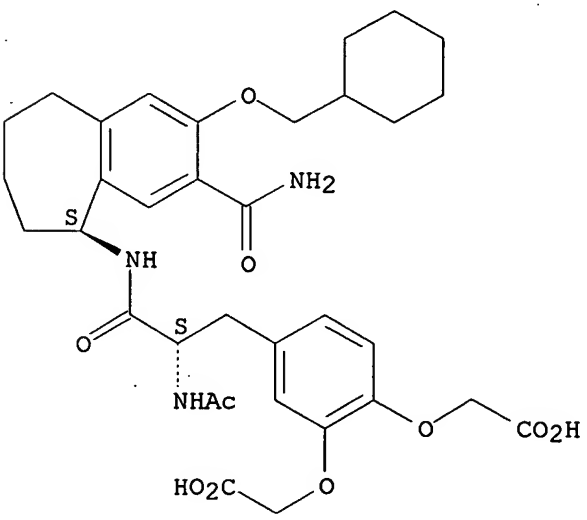
AB R6ZZ1Z2Z3NRR1 [R = H, aliphatic group, (hetero)aryl, etc.; R1 = (un)substituted benzo-fused cycloalkyl or -heterocyclyl; R6 = OH, acyl(oxy), acylalkyl, etc.; Z = (un)substituted phenylene or -naphthylene; Z1 = bond, alkylene, O, (alkyl)imino, etc.; Z2 = bond, alkylene, (alkyl)imino, etc.; Z3 = CO, CH2, SO2, etc.] were prepared as intracellular signal transduction inhibitors (no data). Thus, 6,7,8,9-tetrahydro-5H-benzocyclohepten-2-ol was etherified by bromomethylcyclohexane and the product converted in 9 steps to 9-amino-3-cyclohexylmethoxy-6,7,8,9-tetrahydro-5H-benzocyclohepten-2-carboxamide which was amidated by N-acetyl-L-tyrosine and the product etherified by BrCH2CO2CMe3 to give, after saponification, title compound I.

IT 268741-58-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-benzocycloheptenyl-L-tyrosinamides and analogs as intracellular signal transduction inhibitors)

RN 268741-58-8 CAPLUS

CN Acetic acid, 2,2'-[[4-[(2S)-2-(acetylamino)-3-[[(5S)-3-(aminocarbonyl)-2-(cyclohexylmethoxy)-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-yl]amino]-3-oxopropyl]-1,2-phenylene]bis(oxy)]bis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



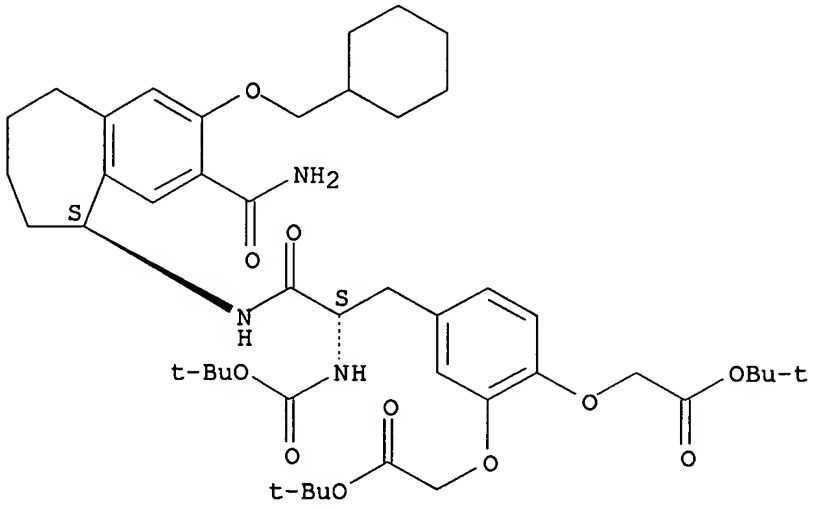
IT 268741-97-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of N-benzocycloheptenyl-L-tyrosinamides and analogs as intracellular signal transduction inhibitors)

RN 268741-97-5 CAPLUS

CN Acetic acid, 2,2'-[[4-[(2S)-3-[[(5S)-3-(aminocarbonyl)-2-(cyclohexylmethoxy)-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-yl]amino]-2-[[(1,1-dimethylethoxy)carbonyl]amino]-3-oxopropyl]-1,2-phenylene]bis(oxy)]bis-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 12 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:184222 CAPLUS

DOCUMENT NUMBER: 130:223585

TITLE: Preparation of substituted phenylalanine derivatives as protein tyrosine phosphatase inhibitors

INVENTOR(S): Larsen, Scott D.; May, Paul D.; Bleasdale, John; Liljebris, Charlotta; Schostarez, Heinrich Josef; Barf, Tjeerd

PATENT ASSIGNEE(S): Pharmacia & Upjohn Company, USA

SOURCE: PCT Int. Appl., 182 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9911606	A2	19990311	WO 1998-US17327	19980824
WO 9911606	A3	19990708		

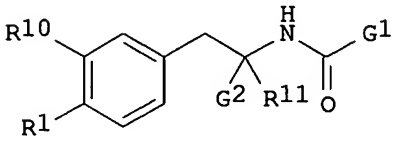
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

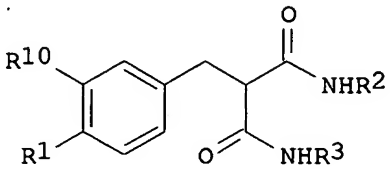
CA 2298601	AA	19990311	CA 1998-2298601		19980824
AU 9892010	A1	19990322	AU 1998-92010		19980824
AU 749132	B2	20020620			
EP 1019364	A2	20000719	EP 1998-944476		19980824
EP 1019364	B1	20040609			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
JP 2001514245	T2	20010911	JP 2000-508647		19980824
AT 268750	E	20040615	AT 1998-944476		19980824
PRIORITY APPLN. INFO.:			US 1997-57730P	P	19970828
			WO 1998-US17327	W	19980824

OTHER SOURCE(S): MARPAT 130:223585

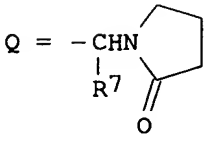
GI

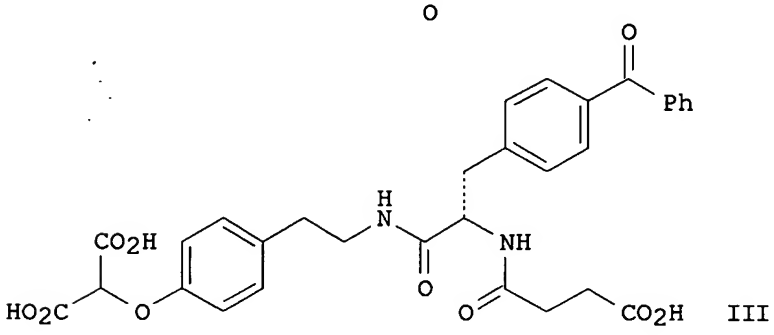


I



II





III

AB The present invention comprises title compds. I and II [G1 = R2, NR8R4; G2 = H, CONHR3, CH2OH, CH:CHR3; R1 = OSO3H, OCH(CO2R5)2, OCH2CO2R5, OCH(CO2R5)CH2CO2R5, O(CO2R5):CHCO2R5, CH2CH(CO2R5)2, CH:C(CO2R5)2, OCH2CONHOH, N(CH2CO2R5)2, OCHFCO2R5; R2 = C1-10 alkyl, C3-8 cycloalkyl, C0-6 alkylphenyl each substituted with 0-2 CO2R5 groups or 0-1 CONH2 groups, CHR7NHXR6, group Q; R3 = (un)substituted C1-12 alkyl, C1-4 alkyl-C3-6 cycloalkyl, C2-12 alkenyl, C3-12 alkynyl, (un)substituted C0-10 alkyl(G3)n, CH(CONH2)-C1-12 alkyl; R4 = H, C1-18 alkyl,alkenyl, C0-6 alkyl-G3; R5 = H, C1-10 alkyl, C1-5 alkylphenyl; R6 = C1-10 alkyl, substituted C1-6 alkyl; R7 = H, substituted C1-6 alkyl; R8 = C0-6 alkyl-G3, CHR7CO2R5, CHR7CH2CO2R5, CHR7CONHCH2COR5; G3 = (un)substituted Ph, naphthyl, heterocyclyl; R10 = H, CO2R5, CONHOH, 5-tetrazolyl, F, OCH2CO2R5; R11 = H, Me; X = CO, SO2, CO2; n = 0-3; with provisos] and pharmaceutically acceptable salts thereof, as small mol. weight, non-peptidic inhibitors of protein tyrosine phosphatase 1 (PTP1) which are useful for the treatment and/or prevention of non-insulin dependent diabetes mellitus (NIDDM). Thus, O-alkylation of N-tert-butoxycarbonyltyramine with di-Et

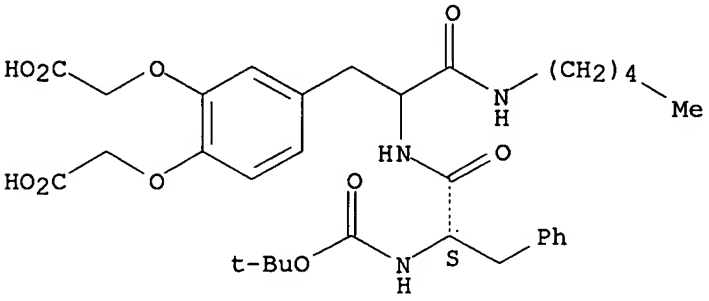
chloromalonate, followed by acidic deprotection, amidation with 4-benzoyl-N-tert-butoxycarbonyl-L-phenylalanine, acidic deprotection, and amidation with succinic anhydride, gave desired title compound III (PNU 176073). III showed 60% inhibition of protein tyrosine phosphatase 1B at a concentration of 10 μM.

IT 221076-92-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted phenylalanine derivs. as protein tyrosine phosphatase inhibitors)

RN 221076-92-2 CAPLUS

CN Tyrosinamide, N-[(1,1-dimethylethoxy)carbonyl]-L-phenylalanyl-3-(carboxymethoxy)-O-(carboxymethyl)-N-pentyl- (9CI) (CA INDEX NAME)

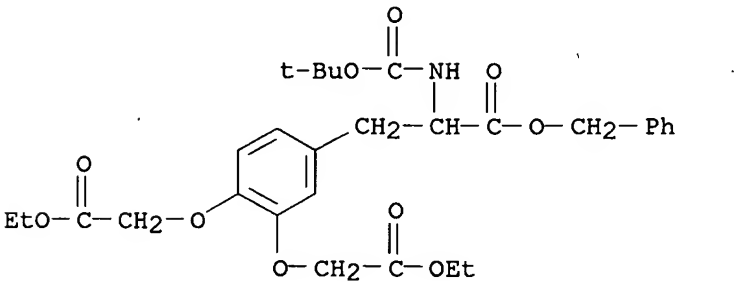
Absolute stereochemistry.



IT 221077-95-8P 221077-97-0P 221077-98-1P
221077-99-2P 221078-02-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of substituted phenylalanine derivs. as protein tyrosine phosphatase inhibitors)

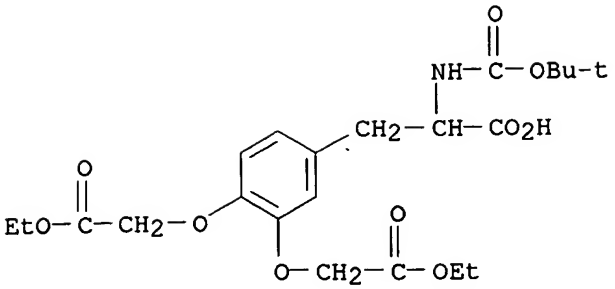
RN 221077-95-8 CAPLUS

CN Tyrosine, N-[(1,1-dimethylethoxy)carbonyl]-3-(2-ethoxy-2-oxoethoxy)-O-(2-ethoxy-2-oxoethyl)-, phenylmethyl ester (9CI) (CA INDEX NAME)

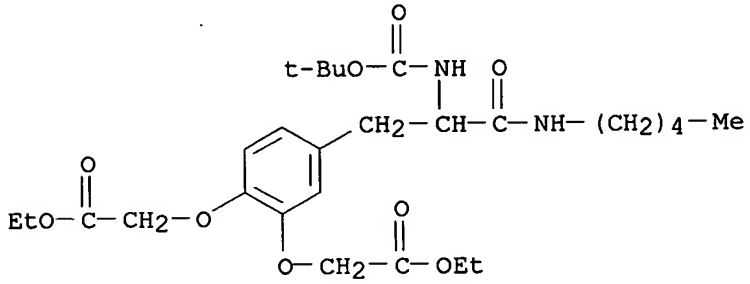


RN 221077-97-0 CAPLUS

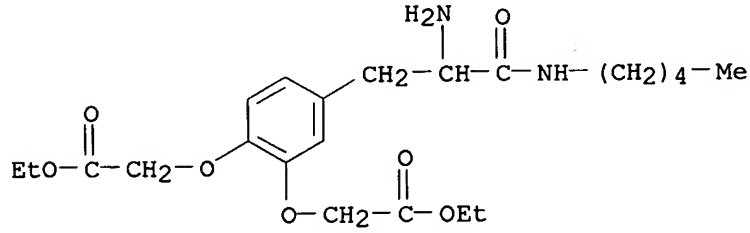
CN Tyrosine, N-[(1,1-dimethylethoxy)carbonyl]-3-(2-ethoxy-2-oxoethoxy)-O-(2-ethoxy-2-oxoethyl)- (9CI) (CA INDEX NAME)



RN 221077-98-1 CAPLUS
CN Acetic acid, 2,2'-[[4-[2-[[(1,1-dimethylethoxy)carbonyl]amino]-3-oxo-3-(pentylamino)propyl]-1,2-phenylene]bis(oxy)]bis-, diethyl ester (9CI) (CA INDEX NAME)

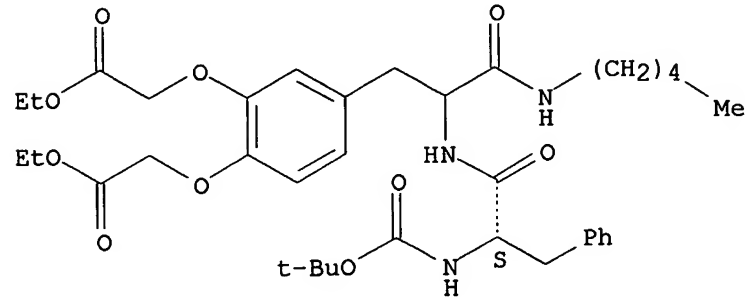


RN 221077-99-2 CAPLUS
CN Acetic acid, 2,2'-[[4-[2-amino-3-oxo-3-(pentylamino)propyl]-1,2-phenylene]bis(oxy)]bis-, diethyl ester (9CI) (CA INDEX NAME)



RN 221078-02-0 CAPLUS
CN Tyrosinamide, N-[(1,1-dimethylethoxy)carbonyl]-L-phenylalanyl-3-(2-ethoxy-2-oxoethoxy)-O-(2-ethoxy-2-oxoethyl)-N-pentyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L11 ANSWER 13 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:768650 CAPLUS
DOCUMENT NUMBER: 130:153950
TITLE: Potent Inhibition of Grb2 SH2 Domain Binding by Non-Phosphate-Containing Ligands
AUTHOR(S): Yao, Zhu-Jun; King, C. Richter; Cao, Tin; Kelley, James; Milne, George W. A.; Voigt, Johannes H.; Burke, Terrence R., Jr.
CORPORATE SOURCE: Laboratory of Medicinal Chemistry Division of Basic Sciences National Cancer Institute, National Institutes of Health, Bethesda, MD, 20892, USA
SOURCE: Journal of Medicinal Chemistry (1999), 42(1), 25-35
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

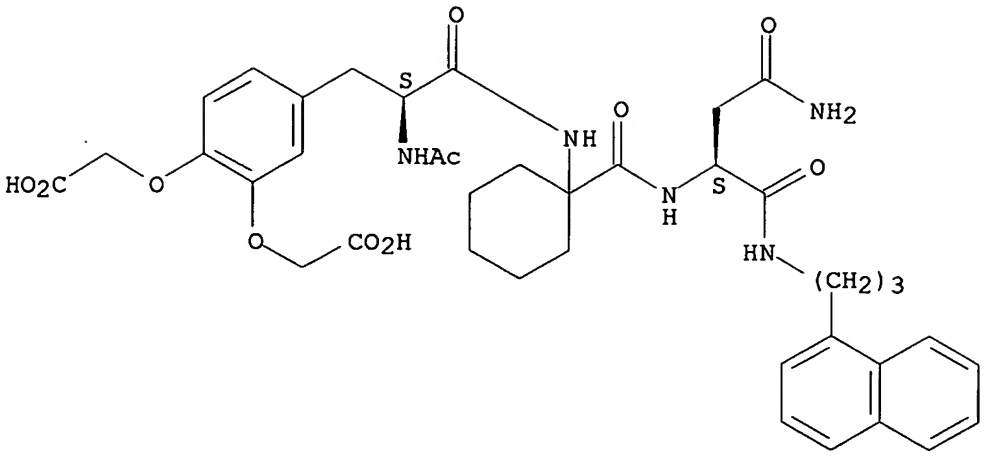
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Development of Grb2 Src homol. 2 (SH2) domain binding inhibitors has important implications for treatment of a variety of diseases, including several cancers. In cellular studies, inhibitors of Grb2 SH2 domain binding have to date been large, highly charged peptides which relied on special transport devices for cell membrane penetration. Work presented in the current study examines a variety of phosphotyrosine (pTyr) mimetics in the context of a high-affinity Grb2 binding platform. Among the analogs studied are new nonphosphorus-containing pTyr mimetics I (R = Ac, COCO2H) which, when incorporated into tripeptide structures II, are able to inhibit Grb2 SH2 domain binding with affinities among the best yet reported for non-phosphorus-containing SH2 domain inhibitors (IC50 values of 6.7 and 1.3 μM, resp.). The present study has also demonstrated the usefulness of the Nα-oxalyl group as an auxiliary which enhances the binding potency of both phosphorus- and non-phosphorus-containing pTyr mimetics. When combined with the (phosphonomethyl)phenylalanine (Pmp) residue to give analogs such as III, potent inhibition of Grb2 SH2 domain binding can be achieved both in extracellular assays using isolated Grb2 SH2 domain protein and in intracellular systems measuring the association of endogenous Grb2 with its cognate p185erbB-2 ligand. These latter effects can be achieved at micromolar to submicromolar concns. without prodrug derivatization. The oxalyl-containing pTyr mimetics presented in this study should be of general usefulness for the development of other Grb2 SH2 domain antagonists, independent of the β-bend-mimicking platform utilized for their display.

IT 220193-79-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of nonphosphate-containing tyrosine ligands as potent inhibitors of Grb2 SH2 domain binding)

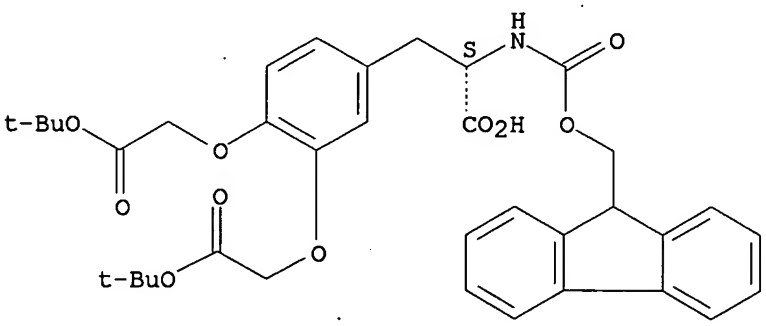
RN 220193-79-3 CAPLUS
CN L-Aspartamide, N-acetyl-3-(carboxymethoxy)-O-(carboxymethyl)-L-tyrosyl-1-aminocyclohexanecarbonyl-N1-[3-(1-naphthalenyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



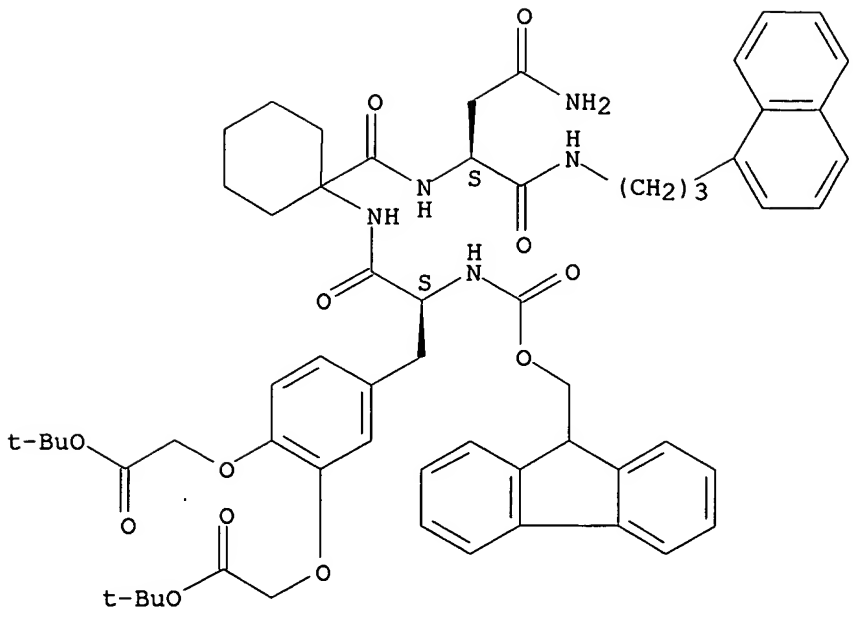
IT 213757-63-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of nonphosphate-containing tyrosine ligands as potent inhibitors of
Grb2 SH2 domain binding)
RN 213757-63-2 CAPLUS
CN L-Tyrosine, 3-[2-(1,1-dimethylethoxy)-2-oxoethoxy]-O-[2-(1,1-dimethylethoxy)-2-oxoethyl]-N-[(9H-fluoren-9-ylmethoxy)carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



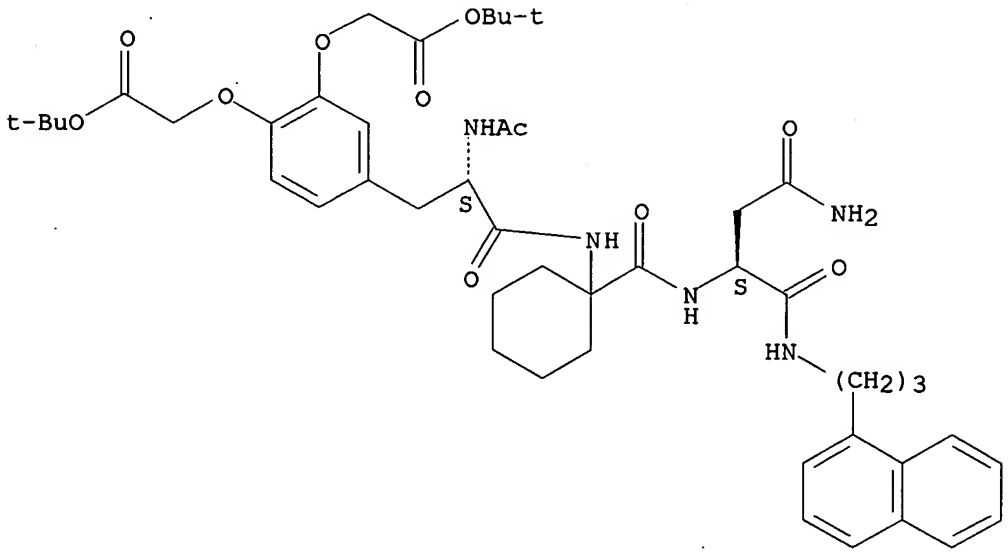
IT 220193-62-4P 220193-73-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of nonphosphate-containing tyrosine ligands as potent inhibitors of
Grb2 SH2 domain binding)
RN 220193-62-4 CAPLUS
CN L-Aspartamide, 3-[2-(1,1-dimethylethoxy)-2-oxoethoxy]-O-[2-(1,1-dimethylethoxy)-2-oxoethyl]-N-[(9H-fluoren-9-ylmethoxy)carbonyl]-L-phenylalanyl-1-aminocyclohexanecarbonyl-N1-[3-(1-naphthalenyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 220193-73-7 CAPLUS
CN L-Aspartamide, N-acetyl-3-[2-(1,1-dimethylethoxy)-2-oxoethoxy]-O-[2-(1,1-dimethylethoxy)-2-oxoethyl]-L-tyrosyl-1-aminocyclohexanecarbonyl-N1-[3-(1-naphthalenyl)propyl]- (9CI) (CA INDEX NAME)

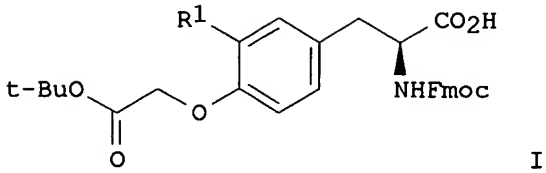
Absolute stereochemistry.



REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 14 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:517177 CAPLUS
DOCUMENT NUMBER: 129:276284
TITLE: Enantioselective synthesis of nonphosphorus-containing phosphotyrosyl mimetics and their use in the preparation of tyrosine phosphatase inhibitory peptides
AUTHOR(S): Burke, Terrence R., Jr.; Yao, Zhu-Jun; Zhao, He;

Milne, George W. A.; Wu, Li; Zhang, Zhong-Yin; Voigt, Johannes H.
CORPORATE SOURCE: Lab. Med. Chem., Div. Basic Sci., Natl. Cancer Inst., Natl. Inst. Health, Bethesda, MD, 20892, USA
SOURCE: Tetrahedron (1998), 54(34), 9981-9994
CODEN: TETRAB; ISSN: 0040-4020
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 129:276284
GI



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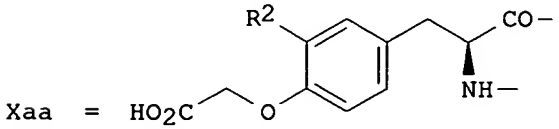


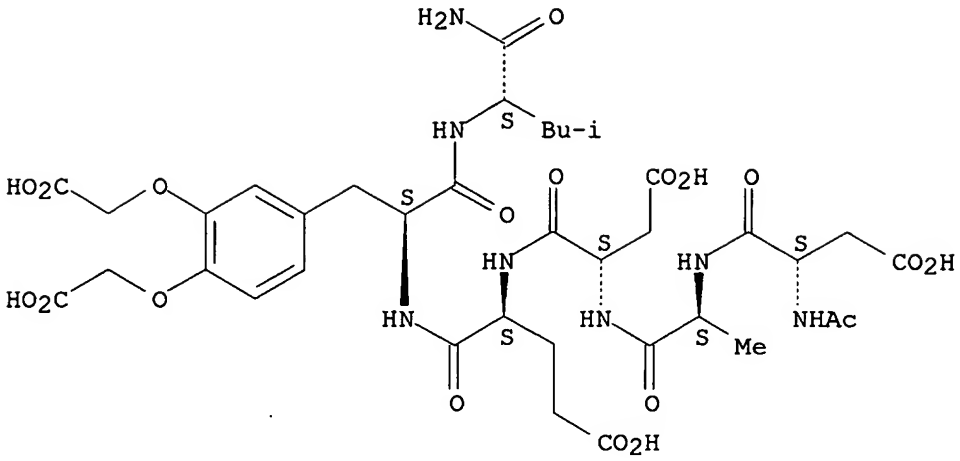
AB Three new L-amino acid analogs I [R1 = H, Me3CO2CCH2O, Me3Si(CH2)2O2C; Fmoc = 9-fluorenylmethoxycarbonyl] have been prepared in protected form suitable for incorporation into peptides by solid-phase synthesis using Fmoc protocols. These agents represent non-phosphorus-containing phosphotyrosyl (pTyr) mimetics, which utilize carboxylic groups to provide functionality normally afforded by the pTyr phosphate group. To demonstrate the utility of these analogs, the protein-tyrosine phosphatase-directed peptides Ac-Asp-Ala-Asp-Glu-Xaa-Leu-NH2 (II) were prepared, where Xaa (R2 = H, HO2CCH2O, HO2C) is a pTyr mimetic. A Ki value of 3.6 μM was obtained against PTP1 for peptide II (R2 = HO2C), which equals the Km of the parent pTyr containing peptide. Besides tyrosine phosphatases, these analogs may be useful in a number of contexts, including SH2 domain and phosphotyrosine binding domain systems.

IT 213757-74-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis of nonphosphorus-containing phosphotyrosyl mimetics for use in the preparation of tyrosine phosphatase inhibitory peptides)

RN 213757-74-5 CAPLUS

CN L-Leucinamide, N-acetyl-L-α-aspartyl-L-alanyl-L-α-aspartyl-L-α-glutamyl-3-(carboxymethoxy)-O-(carboxymethyl)-L-tyrosyl- (9CI) (CA INDEX NAME)

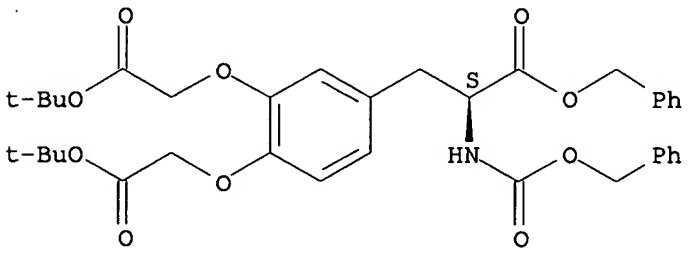
Absolute stereochemistry.



IT 213757-61-0P 213757-62-1P 213757-63-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of nonphosphorus-containing phosphotyrosyl mimetics for use in the preparation of tyrosine phosphatase inhibitory peptides)

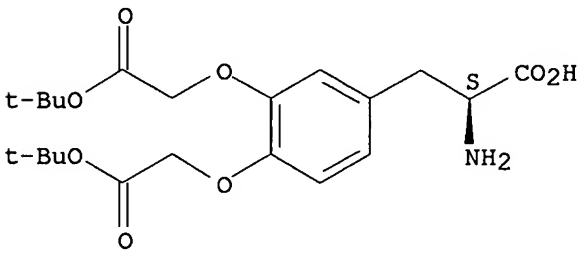
RN 213757-61-0 CAPLUS
CN L-Tyrosine, 3-[2-(1,1-dimethylethoxy)-2-oxoethoxy]-O-[2-(1,1-dimethylethoxy)-2-oxoethyl]-N-[(phenylmethoxy)carbonyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



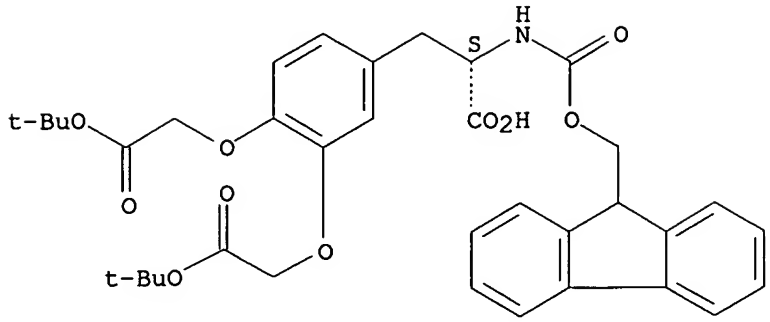
RN 213757-62-1 CAPLUS
CN L-Tyrosine, 3-[2-(1,1-dimethylethoxy)-2-oxoethoxy]-O-[2-(1,1-dimethylethoxy)-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 213757-63-2 CAPLUS
CN L-Tyrosine, 3-[2-(1,1-dimethylethoxy)-2-oxoethoxy]-O-[2-(1,1-dimethylethoxy)-2-oxoethyl]-N-[(9H-fluoren-9-ylmethoxy)carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

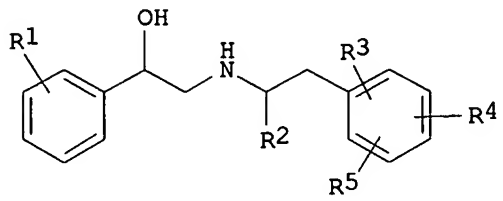


REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

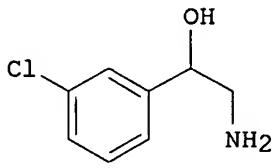
L11 ANSWER 15 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:394205 CAPLUS
DOCUMENT NUMBER: 127:33994
TITLE: Preparation of phenylethanol amine derivatives for treatment of diabetes, high blood glucose, and obesity diseases
INVENTOR(S): Inomata, Kohei; Oshida, Norio; Kubota, Nobutoshi; Iwata, Naohito; Hamada, Tamiko; Takahashi, Toshihiro
PATENT ASSIGNEE(S): Nisshin Flour Milling Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 34 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 09118655	A2	19970506	JP 1996-209379	19960722
PRIORITY APPLN. INFO.:			JP 1995-232093 A	19950818
OTHER SOURCE(S):	MARPAT 127:33994			

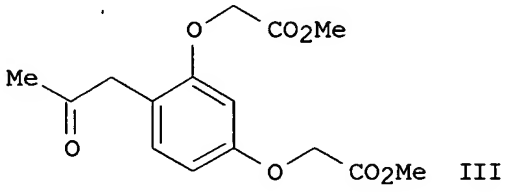
GI



I



II



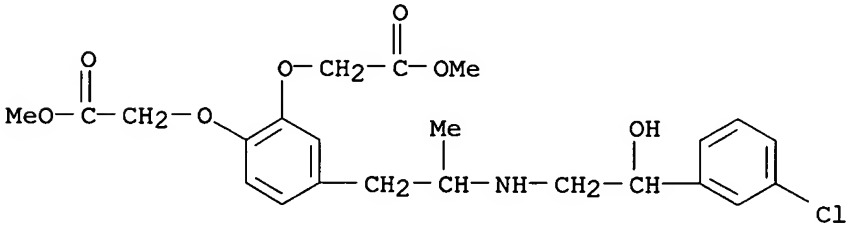
III

AB The title compds. (I; R1 = H, halo; R2, R6 = H, C1-4 alkyl; R3-R5 = H, OCH2CO2R6) are prepared I are useful for prevention and treatment of

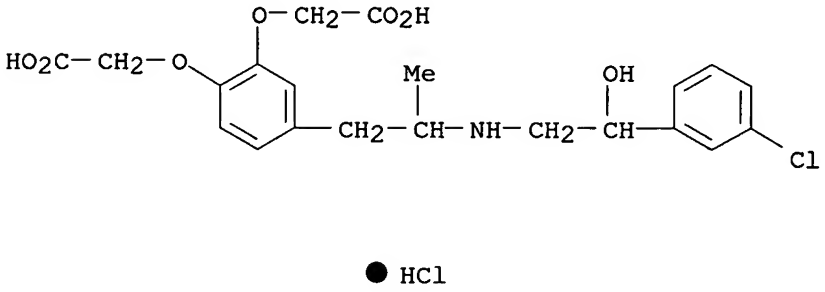
diabetes, high blood glucose, and obesity diseases and as texture improvement agents for flesh animals. Thus, benzyl alc. derivative (II) was refluxed with benzene derivative (III) in C6H6 and then hydrogenated over PtO2 to give 52% I(R1 = R4 = H, R2 = Me, R3 = 2-OCH2CO2Me, R5 = 4-OCH2CO2Me) (IV). IV showed fat disassembly activity (β3) EC50 of 9.0 X 10-8 M when tested on rats. A tablet and granule formulation containing IV were prepared

IT 190372-40-8P 190372-41-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of phenylethanol amine derivs. for treatment of diabetes, high blood glucose, and obesity diseases)

RN 190372-40-8 CAPLUS
CN Acetic acid, 2,2'-[[4-[2-[[2-(3-chlorophenyl)-2-hydroxyethyl]amino]propyl]-1,2-phenylene]bis(oxy)]bis-, dimethyl ester (9CI) (CA INDEX NAME)



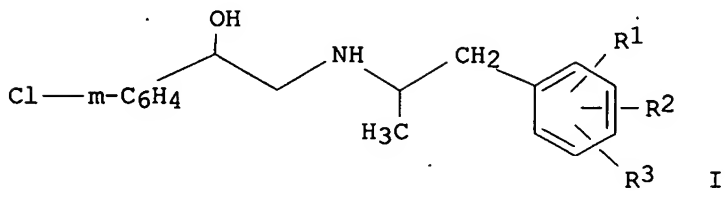
RN 190372-41-9 CAPLUS
CN Acetic acid, 2,2'-[[4-[2-[[2-(3-chlorophenyl)-2-hydroxyethyl]amino]propyl]-1,2-phenylene]bis(oxy)]bis-, hydrochloride (9CI) (CA INDEX NAME)



L11 ANSWER 16 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:663105 CAPLUS
DOCUMENT NUMBER: 123:74912
TITLE: Preparation of phenylethanolamine derivatives and antiobesity agents and antidiabetic agents containing them
INVENTOR(S): Okuyama, Akihiko; Tanaka, Shimizu; Nagahara, Michiko; Uchida, Katsuhiro; Muraoka, Yuriko; Watanuki, Mitsuru; Shimada, Shuji
PATENT ASSIGNEE(S): Kaken Pharma Co Ltd, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 10 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 07112958	A2	19950502	JP 1993-280041	19931013
PRIORITY APPLN. INFO.:			JP 1993-280041	19931013
OTHER SOURCE(S):	MARPAT 123:74912			

GI



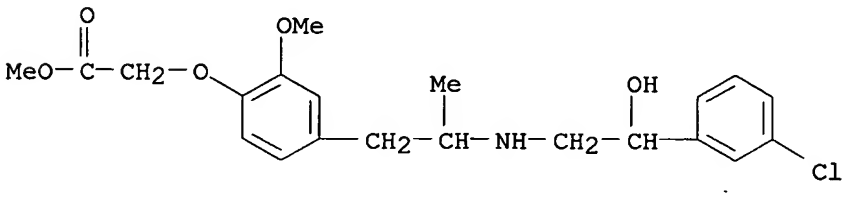
I

AB The title derivs. I (R1-2 = H, halo, C1-4 alkyl, C1-4 alkoxy: R3 = OCR4R5CO2R6; R4 = H, C1-13 alkyl, aryl; R5-6 = H, C1-4 alkyl) or their pharmaceutically acceptable salts and antiobesity agents and antidiabetic agents containing I or their salts are claimed. 3-ClC6H4CH(OH)CH2NH2 was treated with 1-[4-(1-ethoxycarbonylethoxy)phenyl]propan-2-one in benzene under reflux for 4 h. After removal of benzene the reaction product in MeOH was treated with gradual addition of NaBH4 at 0° and the reaction mixture was further stirred at 0° for 30 min to give 67.7% I (R1 = R2 = H, R3 = OCHMeCO2Et) (II). ED50 value of β3-agonistic action of II, i.e. promotion of lipolysis by adipose cell, was 10 nM, vs. 1.7 nM of BRL-35135. ED50 values of β1- and β2-agonistic actions of II were 828 and 2.2 nM. I (R1 = H, R2 = 3-Me, R3 = 4-OCH2CO2Me) showed antiobesity effect on Na glutamate-induced obese mice.

IT 164984-13-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(N-(phenylmethylethyl)hydroxyphenylethanamines with β3-agonistic action and antiobesity and antidiabetic agents containing them)

RN 164984-13-8 CAPLUS

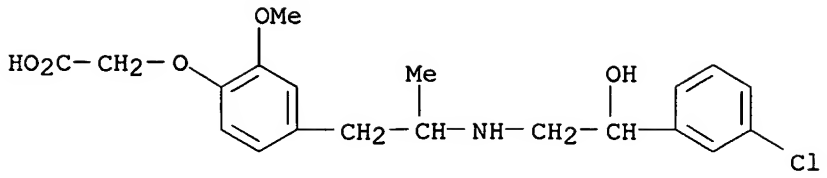
CN Acetic acid, [4-[2-[[2-(3-chlorophenyl)-2-hydroxyethyl]amino]propyl]-2-methoxyphenoxy]-, methyl ester (9CI) (CA INDEX NAME)



IT 164984-14-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(N-(phenylmethylethyl)hydroxyphenylethanamines with β3-agonistic action and antiobesity and antidiabetic agents containing them)

RN 164984-14-9 CAPLUS

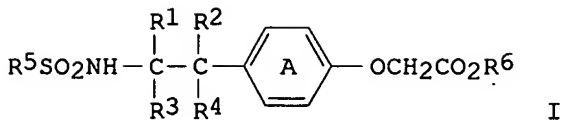
CN Acetic acid, [4-[2-[[2-(3-chlorophenyl)-2-hydroxyethyl]amino]propyl]-2-methoxyphenoxy]- (9CI) (CA INDEX NAME)



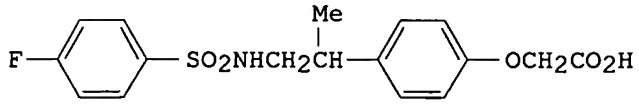
L11 ANSWER 17 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1988:422655 CAPLUS
DOCUMENT NUMBER: 109:22655
TITLE: Preparation of (arylsulfonylaminoalkyl)phenoxyacetic acid derivatives useful for treating or preventing thrombotic diseases or embolism
INVENTOR(S): Iwakuma, Takeo; Kawaguchi, Takayuki; Yamashita, Toyoharu; Sasaki, Yasuhiko; Shimazaki, Tamotu
PATENT ASSIGNEE(S): Tanabe Seiyaku Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 44 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
EP 255728	A2	19880210	EP 1987-111402		19870806
EP 255728	A3	19890510			
EP 255728	B1	19911127			
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE					
IL 83230	A1	19920621	IL 1987-83230		19870717
CA 1277675	A1	19901211	CA 1987-543552		19870731
JP 64000062	A2	19890105	JP 1987-194811		19870804
JP 04057669	B4	19920914			
DK 8704089	A	19880207	DK 1987-4089		19870805
NO 8703272	A	19880208	NO 1987-3272		19870805
NO 166938	B	19910610			
NO 166938	C	19910918			
AU 8776596	A1	19880211	AU 1987-76596		19870805
AU 597707	B2	19900607			
ZA 8705784	A	19880427	ZA 1987-5784		19870805
HU 45230	A2	19880628	HU 1987-3579		19870805
SU 1614760	A3	19901215	SU 1987-4203067		19870805
FI 8703413	A	19880207	FI 1987-3413		19870806
FI 87769	B	19921113			
FI 87769	C	19930225			
CN 87105501	A	19880217	CN 1987-105501		19870806
CN 1011780	B	19910227			
AT 69807	E	19911215	AT 1987-111402		19870806
ES 2038630	T3	19930801	ES 1987-111402		19870806
AT 8702623	A	19921115	AT 1987-2623		19871008
AT 396235	B	19930726			
US 4866196	A	19890912	US 1988-141403		19880104
SU 1748643	A3	19920715	SU 1988-4356064		19880712
PRIORITY APPLN. INFO.:			JP 1986-184693	A	19860806
			JP 1987-26858	A	19870206
			US 1987-80676	A1	19870731
			EP 1987-111402	A	19870806

OTHER SOURCE(S): CASREACT 109:22655; MARPAT 109:22655
GI



I



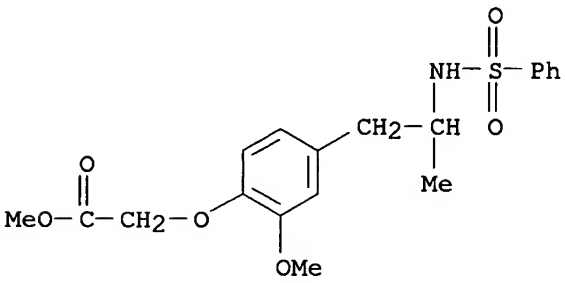
II

AB The title compds. [I; ring A may have 1-2 substituents selected from alkyl, alkoxy, halo; 1 or 2 of R1-R4 = alkyl, others = H; R5 = Ph (un)substituted by 1-3 groups selected from alkyl, halo, alkoxy, trihalomethyl, NO2; R6 = H, protecting group [e.g., alkyl, (un)substituted phenylalkyl]] are prepared for use in the treatment or prophylaxis of thrombotic diseases or embolism. Acylation of (±)-[4-(2-amino-1-methylethyl)phenoxy]acetic acid by 4-FC6H4SO2Cl in aqueous K2CO3 at 80° gave [(fluorophenyl)sulfonylaminoethyl]phenoxyacetic acid (±)-II, as its Na salt, in 60% yield. The chloro analog of (±)-II had an IC50 of 0.5 μg/mL for inhibiting collagen-induced platelet aggregation in vitro, vs. 2 μg/mL for 4-(PhSO2NHCH2CH2)C6H4OCH2CO2H.

IT 114963-26-7P 114986-64-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as antithrombotic)

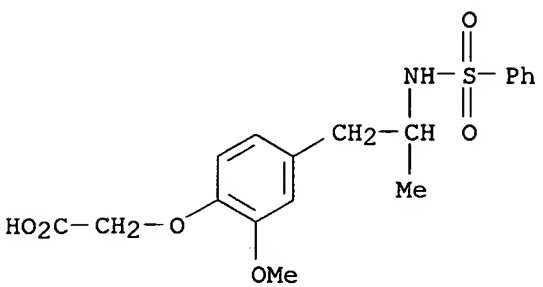
RN 114963-26-7 CAPLUS

CN Acetic acid, [2-methoxy-4-[2-[(phenylsulfonyl)amino]propyl]phenoxy]-, methyl ester (9CI) (CA INDEX NAME)



RN 114986-64-0 CAPLUS

CN Acetic acid, [2-methoxy-4-[2-[(phenylsulfonyl)amino]propyl]phenoxy]- (9CI) (CA INDEX NAME)



L11 ANSWER 18 OF 18 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1972:462312 CAPLUS
DOCUMENT NUMBER: 77:62312
TITLE: L-Dopa derivatives
INVENTOR(S): Kaiser, Ado; Koch, Wolfgang; Scheer, Marcel; Woelcke, Uwe
PATENT ASSIGNEE(S): Hoffmann-La Roche, F., und Co., A.-G.
SOURCE: Ger. Offen., 61 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

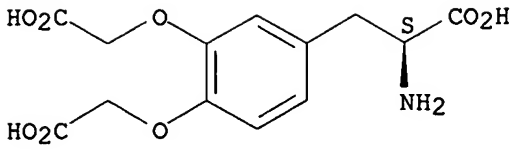
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2153800	A	19720504	DE 1971-2153800	19711028
CH 562199	A	19750530	CH 1970-16048	19701030
ZA 7105981	A	19720628	ZA 1971-5981	19710907
AU 7133318	A1	19730315	AU 1971-33318	19710909
IL 37704	A1	19751015	IL 1971-37704	19710913
FR 2111942	A5	19720609	FR 1971-38773	19711028
FR 2111942	B1	19750801		
BE 774678	A1	19720502	BE 1971-109925	19711029
NL 7114948	A	19720503	NL 1971-14948	19711029
GB 1347375	A	19740220	GB 1971-50335	19711029
CA 996131	A1	19760831	CA 1971-126428	19711029
SE 7506820	A	19750613	SE 1975-6820	19750613
SE 7506821	A	19750613	SE 1975-6821	19750613

PRIORITY APPLN. INFO.: CH 1970-16048 A 19701030

AB About 50 L-3,4-(R2O)2C6H3CH2(NHR1)CO2R [I, R = H, Me, Et, Bu, PhCH2, allyl, MeCH:CHCH2, R1 = tert-BuO2C, PhCH2O2C, Ac, o-O2NC6H4S, R2 = H, allyl, MeCH:CHCH2, EtO2C, EtO2CCH2, HO2CCH2, Bz, MeSO2, Me2NCO, CH2:CHCO, CH.tplbond.-CCH2, Me(CH2)nCO (n = 0-6)] and their HCl salts or oxalates, hypotensive, antipyretic, or antiparkinsonism agents, were prepared by acetylation or esterification of I (R = R2 = H), reaction of I (R2 = H) with R2Cl or R2Br, cleavage of R1 by hydrolysis with HCl or hydrogenation, resp., and cleavage of R by hydrolysis with NaOH or HCl. Thus, I (R = R2 = H, R1 = tert-BuO2C = Q) was treated with CH2N2 in Et2O to give I (R = Me, R1 = Q, R2 = H). This was refluxed for 14 hr with CH2:-CHCH2Br in Me2CO in the presence of K2CO3 under argon to give I (R = Me, R1 = Q, R2 = allyl) (II). II was saponified with aqueous NaOH in dioxane for 14 hr at room temperature to give I (R = H, R1 = Q, R2 = allyl). This was treated with HCl in AcOH to give I.HCl (R = R1 = H, R2 = allyl). I (R = R1 = H) were pharmaceuticals.

IT 37168-64-2P 37169-48-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 37168-64-2 CAPLUS
CN L-Tyrosine, 3-(carboxymethoxy)-O-(carboxymethyl)-, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

RN 37169-48-5 CAPLUS
CN L-Tyrosine, N-acetyl-3-(2-ethoxy-2-oxoethoxy)-O-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.